15

# Vasculitis

def. Specific pattern of inflammation of the BVs wall That Can affect any body system & has clinical finding ranging from: Erythema & urticaria to purpura, Necrosis, & ulceration

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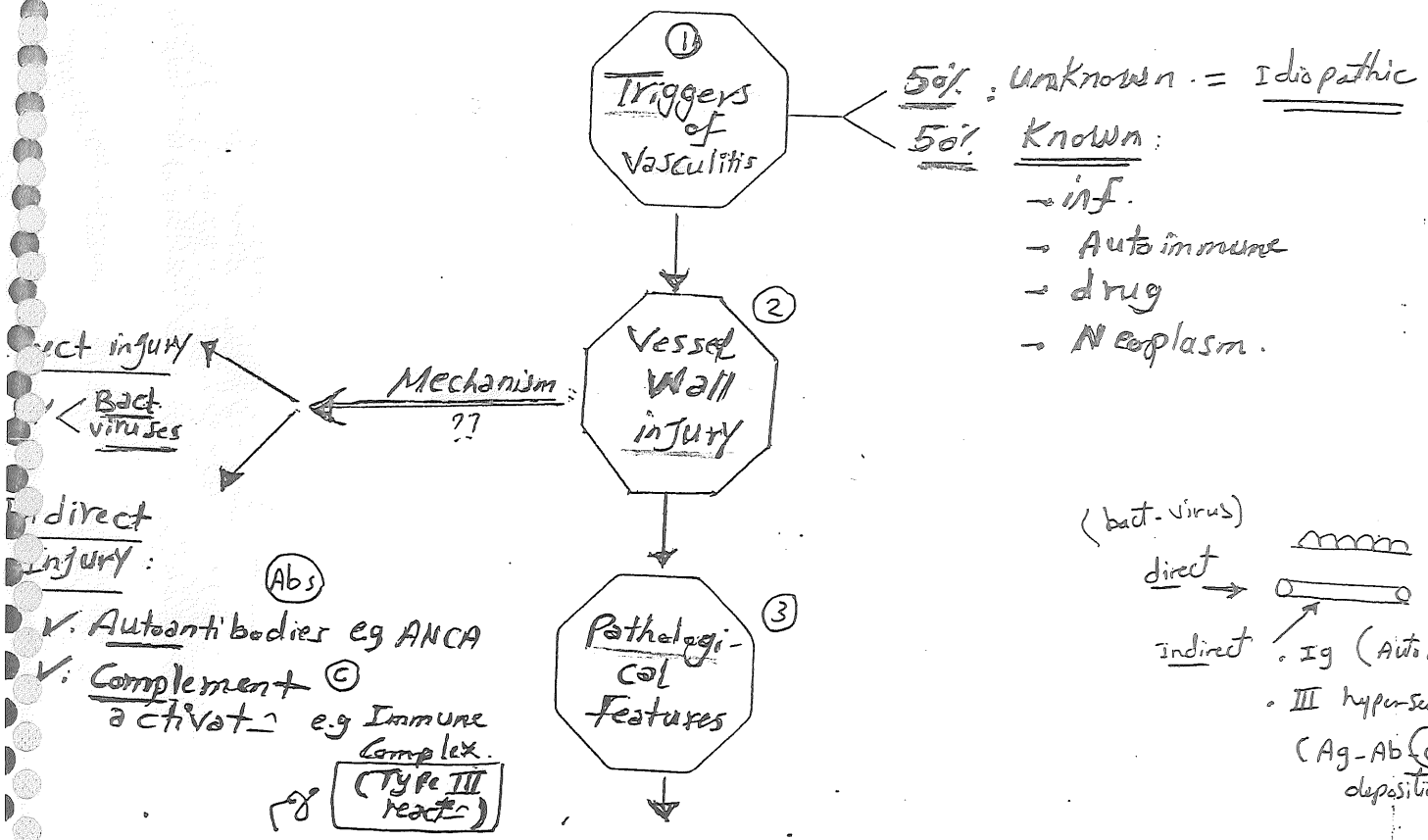
## Pathogenesis of Vasculitis




## Pathological features of (HIP) Vasculitis. (Triad). △

H/p * Vasculitis :-

(2)

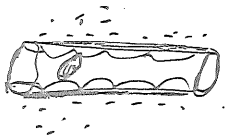
△ ① Fibrinoid Necrosis ← Endothelial swelling + Fibrin deposit (Eosinophilic strands) in & around Vs Wall → Smudgy appearance

wall

of ② Perivascular Infilt ← inhilt inflamm destruction of bl. vs wall

③ Less essential features :-

- Edema
- RBCs extravasation
- Vs Wall infilt.
- Luminal thrombus.
- Leukocytoclasia ✓



* Vasculopathy = pseudo vasculitis :-

- Fibrinoid deposit ↑ ē (No) inflammation
- Vs Wall infilt ē ± (No) alterat- (minimal)
- Leukocytoclasis ē (out) fibrinoid degen.

(NB)

Type (I) hypersensitivity → urticaria

(II) → drugs

(III) → vasculitis

(IV) → CMI (as) Contact dermatitis (CD)

Serious drug :-

- Allopurinol
- Septrine
- Anti Convalsant.

## Histopathological features are essential for Dx of Vasculitis (3 CVs)

1. Fibrinoid degen. (or) Necrosis: endothelial inflamm + fibrin deposits in & around / Vs Wall → Eosinophilic strands (E) smudgy appearance of BVs.
2. Angio centric (perivascular) (or) Angio invasive (Vascular Wall) infiltrates.
3. Vs Wall disrupt^ (or) destruct^

NB: Non essential features → Edema, Ulcerat^, RBCs extrav.

Q الفرق بين Vasculitis & Vasculopathy

Vasculopathy: Fibrin deposit^, Thrombosis, Vs Wall infiltration without disrupt^ or destruct^ (No inflamm) (No fibrinoid degeneration)

### Classificat^ of Vasculitis: (No) universally Accepted Classificat^):

- Cutc: < 4ws — purpura, ulcerat^, Systemic manif..
- hyr: (mild) > 4w — macules, papules. No systemic manif.

Classificat^ may be According to:-

1. Size of involved Vs. (Small, Medium, large)
2. Type of infilt.
3. onset: Acute, & chronic.
4. Etiology: (1ry) (Idiopathic) or (2ry) → Inf., Autimmune, Drugs, Mg.
5. Extent: (Cut) (localized) or (Systemic)
   - Cut. affect^ only
   - Systemic organ affect^

### Most Common 3 organs:-

- GIT: NV, abd. pain & (Melena)
- Joint: Arthralgia & Myalgia.
- Renal: HTN, Hematuria & Edema

Others:
- CNS: Parasthesia
- CVS: Chest pain & CHF
- RT: dyspnea & Cough
- General: FAHM

## According to infilt

### ⊡ Lymphocytic
- AICTDs
- EM
- Behcet & PG
- pLEVA
- LYP
- GVHD
- Angiodestructive ← Lymphoma / Lymphoma-Granulomatous

### ⊡ Eosinophilic
- Granuloma facial
- Hyper-Eosinophilic Synd.
- churg Strauss
- ± AICTDs

### ⊡ Granulomatous
- Takayasu
- Giant Cell
- Nodular Vas
- Wegeners
- churg-Strauss

← Eos.
← granula
← IGD

### ⊡ Incidental
- Sweet
- PG

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### 1- Immune Complex Vs
1- predominant IgA ← idiopathic HSP drug infection
2- ~ IgG, IgM → idiopathic, drug infect
3- Mixed cryoglobulinemia
4- Rheumatic Vs asse AICTDs

### 2- PaNG Immune Vs
- ANCA ← MPA WG CSS
- EED
- GF
- Sweet
- Cut PAN
- some pustular Vs

(NB) **Localized Types of Vasculitis**
- EED
- GF

5- some pustular Vs
6- Bn hypergammaglobulinemic purpura of Waldenstrom.

# CHCC 2012 Classification (Acc. to size of BV) (5)

Aorta

**1- Large Vs Vasculitis: (Aorta).**

- Giant Cell arteritis
- Takayau's arteritis.

deep dermis (50-150 μ) **2. Medium Vs. Vasculitis:** (Affect aa: in deep dermis & S.C.T, Coronary, hepatic) & Renal

- PAN
- [KD] → - Kawasaki's dis. (Coronary not cut Vasculitis) ×

upper dermis (<50 μ) **3 Small Vs Vasculitis:** (arterioles, Capillaries, post Capillary Venules in upper dermis)

↓

2 Types

- **ANCA associated**
  - Wegener's Granulomatosis (WG)
  - Churg - Strauss (CSS) Synd.
  - Microscopic Polyangitis (MPA)
  - Drug induced. - Idiopathic
- **Non ANCA Associated**
  - LCV
  - urticarial Vasculitis (UV)
  - HSP
  - EED
  - Cryoglobulinemia.
  - AHEI

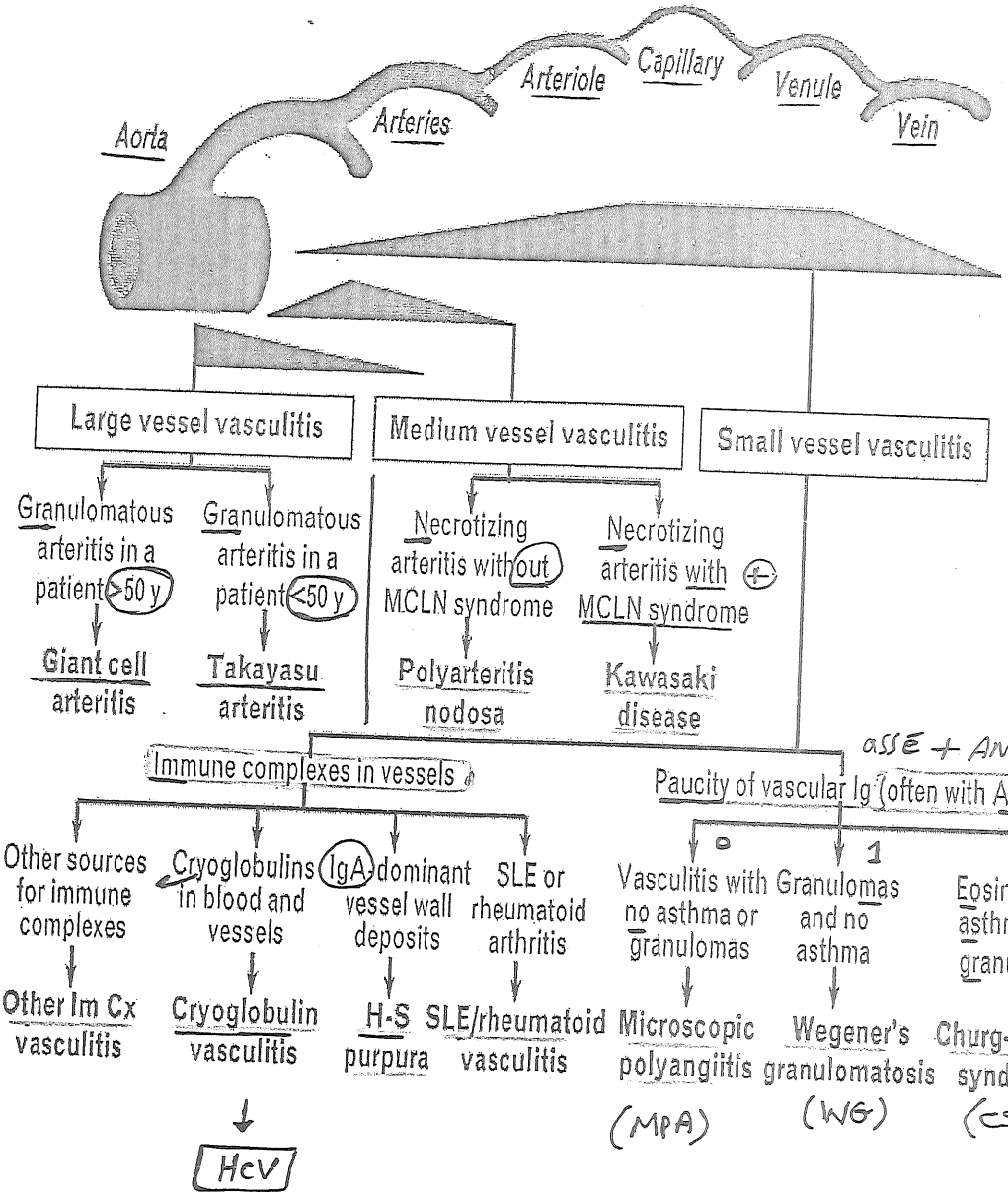
  (2 infant)
  - ENL

**4 Variable Vs Vasculitis**
- Behcet
- Cogan synd.

**5 Vasculitis With systemic dis:**
- Lupus Vasculitis
- Rheumatoid "
- Sarcoid "

**6 Vasculitis ass. & Probable Etiology**
- HCV ass. Cryoglob. / HBV ass / Drug

Small-med. sized
- Cryoglob.
- ANCA Vasculitis


Aorta
Arteries
Arteriole
Capillary
Venule
Vein
Large vessel vasculitis
Medium vessel vasculitis
Small vessel vasculitis
Granulomatous arteritis in a patient >50 y
Giant cell arteritis
Granulomatous arteritis in a patient <50 y
Takayasu arteritis
Necrotizing arteritis without MCLN syndrome
Polyarteritis nodosa
Necrotizing arteritis with MCLN syndrome
Kawasaki disease
Immune complexes in vessels
Paucity of vascular Ig (often with ANCA)
asse + ANCA
Other sources for immune complexes
Other Im Cx vasculitis
Cryoglobulins in blood and vessels
Cryoglobulin vasculitis
HcV
IgA dominant vessel wall deposits
H-S purpura
SLE or rheumatoid arthritis
SLE/rheumatoid vasculitis
Vasculitis with no asthma or granulomas
Microscopic polyangiitis
(MPA)
Granulomas and no asthma
Wegener's granulomatosis
(WG)
Eosinophilia, asthma, and granulomas
Churg-Strauss syndrome
(CSS)

# Small Vs Vasculitis (7)

## 1 - Leukocytoclastic Vasculitis (LCV)

(Cut. SVV [CSVV] // Allergic or Hypersensitivity Vasculitis)

**Def** Small Vs Vasculitis that's ch BY:

- clinically: painful palpable purpura (3P)
- pathologically: Leukocytoclasis (+/-2) → angiocentric / Angio Invasive infilt. Vs wall destruct. ± fibrinoid degen.

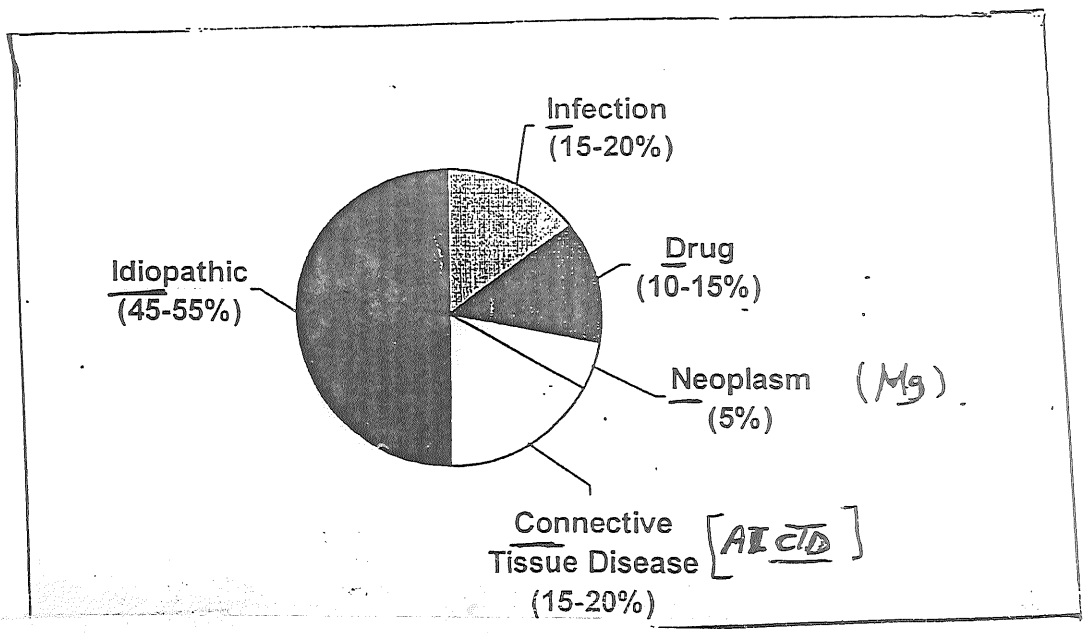
**pathophysiology**: Triggers → Immune Complex deposit (Type III react) → pathological changes of Vasculitis

((Not Lb))

**Etiology**:

Triggers

- 5% Idiopathic → Called (1ry) Vasculitis
- 50% Known causes → See below → Called (2ry) Vasculitis
  - infect
  - Mg
  - drugs
  - AI CTDs



# • Known Causes of Vasculitis:

(8)

## A. Inf: (15-20%)

### 1. Bacterial:

- Staph. (rare)
- Strept
- E. Coli
- Brucella
- Salmonella
- Mycobact.
- Chlamydia.

### 2. Viral:

- HCV > HBV > HAV (Also their Vaccines)
- HIV
- VZV (rare).

## B. Autoimmune C.T dis: (15-20%)

← also "IBD"

- SLE
- Sjogren → SS
- RA
- DM

→ Autoantibodies → Vasculitis.

## C Drugs: (10-15%)

أي دوا ممكن يعمل ولكن أشهرهم:

- Antibiotics (Betalactam) (also • Minocycline • Quinolones)
- NSAIDs.
- Thiazide diuretics
- Thiouracil
- Anti Coagulants (Warfarin & Coumarin)
- Anti thyroids
- Anti TNF.

## D Neoplasm (2-5%)

- Leukemia
- Lymphoma
- MM
- Carcinomas.

## E. others: (3F)

1. Genetics:
   - FME
   - Immunodef. Synd
2. Food & its Additives (Tartrazine)

CIP
LCV
± Cut ± systemic

## 1- Cut. manifs. of LCV:

- Bilat.
- Symmetrical

LL = • site → at defendant sites & sites under Tight ("Tying Clothes" بالملابس الضيقة)
• Symptoms: Asymptomatic but ± pain burning or Itching
• Lesion:

**Typically**

3P: Painful, Papable (±) ulcer, Purpura

**Less Common**

- Urticarial like (more in chr. cases)
- Nodules
- Levido Reticularis. (LR)
- Retiform purpura. (Rp)

## 2- Systemic manifs. of LCV: (جدول بولونيا)

اسأل عن الأعراض

(i). Commonest 3 organs affected:-
- GIT → AN - AP - Melena
- Joint → Arthritis - Arthralgia
- Renal → Haematuria - Eodema - HTN.

(ii). Other organs: CNS, CVS, RT, General.
- CNS: paresthesia
- CVS: dyspnea, chest pain
- RT: Cough
- General: FAHM

## Course (prognosis) of LCV:-

(90%) ← 1. Acute LCV = ch. By:

- Severe Cut. affect = (purpura & ulcerat=)
- Mild systemic "

ثم دلوقتي resolut= ē in 4 ws (3-6 ws) [90%]

(10%) ← 2- Chr. (Re current):

- Mild Cut. affect = (macules, papules & urticaria)
- X · (No) systemic "
- Remission & Exacerbat= for > 4 ws. (at) ms-ys intervals.

LCV has good prognosis

∴ So prognosis of LCV is good ē 90% of cases show spontaneous resolut= within 4 ws while 10% will have recurrent (or) chronic dis.

predictors of chronicity:
- Arthralgia
- Cryoglob.
- No fever

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## Evaluation of A Case of LCV (Diagnosis)

لازم يعمل ٤ خطوات

1- Confirm the clinical diagnosis by Histopathology & DIF. .- < HP DIF

2- detect systemic involvement — Syst affect

3- detect the Etiology (in 2ry cases). — AET

**1- Confirm the clinical Dx by Histopath. & DIF:-**

لازم العينة تتأخذ بين ١٢-٢٤ 12-24h

Path → Leukocytoclasia? + Vasculitis (≥ 2 criteria)

- precautions:- ± others.
  - Too early (<12 hr) or too late (>24 hrs) → may be -ve → Biopsy
  - after >24 hrs → -ve (IF)
  - Eosinophils → indicate drug Etiology.

Leukocytoclasia: Neutrophilic degranulation & fragmentation & nuclear dust formation in Dermis (Nuclear karyorrhexis)

DIF: granular deposition of $C_3$, IgG, IgM, IgA at Vs. Wall.

**2 Detection of systemic affection: BY:-**

- Hx: History
- Clp: Clinical Exam.
- Inv: Invst e.g CT, XR, Urine, CBC, ...

**3 Detection of Etiology of Vasculitis:** (in 2ry Type)

(a) Hx of:
- Drug
- inf.
- Food Allergy
- Ass. systemic dis. (AICTDs)

(b) Lab:
- CBC, ESR, ASO
- CRP
- LFT, RFT
- → ANA
- ANCA
- ← Cryoglobulins
- Complement level (pt) ← SLE / UV
- Urine analysis.

(c) Rad.: CT scanning for Possible Mg. ← Cause

# Treatment of LCV

(Should it be aggressive as Majority (90%) of cases are self limiting without systemic manifs.)

- Cut. affect⁻ only
  - Mild cut. (No ulcerat⁻)
    - Supportive Care
      - Antihistamines
      - NSAIDs
    - Pentoxiphylline
    - Dapsone
    - Colchicine.
    - Treatal
    - (2nd line)
  - Severe Cut. (ulcerat⁻) ← أنقصه
    - Thalidomide.
    - MTX (low dose Weekly)
    - prednisone. (Cs)
- systemic affect⁻
  - Cs
  - (Azathiop. / Cyclosporine / Mycophenolate -M.) — Immuno-Sup — 3rd li
  - IFN-
  - IVIG
  - ECP
  - Infliximabe

## ⊙ Supportive Care :-

1- Rest — راحة
2- Leg Elevat⁻ — رفع رجل وتريح
3- Avoid Trauma & Cold — تجنب الصدمات والبرد
4- remove The offending (Ag)

تحويل عيادات:

- باطنة
- كلى
- روماتيزم → AI CTDs = e.g. RA, DM
- صدرية
- عصبية

## 2- Urticarial Vasculitis (UV): (Erythema Elevatum Diutinum)

- Def: recurrent Episodes of painful, persistent (>24hrs) urticarial-like lesions with or without Angioedema (±) (frequent)
- Incid: unknown but (≃ 5-10%) of cases having ordinary urticarial Wheals show UV on pathology.

Female > 30-50y

أعمل circle test ← Wheal دايرة وليه ارسم وانشوف لحد امتى بيعم موجودة وبعدين

- Etiology ① Idiopathic (primary)
② 2ry to:-
  - Inf. (sp. HBV, HCV & EBV)
  - Autoimmune (sp. SLE & SS)
  - Drugs (sp. KI, fluoxetine & NSAIDs)
  - Neoplasms.

- C/P: Urticarial Vasculitis is very similar to Wheals of ordinary Urticaria but differs in:-

1- lesions lasting >24 hrs. (persistant)
2- (Painful) rather than Pruritic. (Burning or)
3- on healing → Postinflamm. Hyperpigm. (PIH)
4 (Path) → (as) LCV.
5 with (diascopy) → Hge (sometimes subtle) can be observed.

However these features not always present. 5-10% of ordinary Urtic. → UV By Hx

# ⊙ Types of Urticarial Vasculitis:-

(14)

## Normocomplementemic (Most cases 70-80%)

- ⊙ Ch By:
  - Mild
  - self limiting
  - affect skin only (No systemic)
- ⊙ NL Complement level.
- ↓ Mild therapy

## Hypocomplementemic (less common) (HUV)

- ⊙ Severe
  - Cut. & Systemic affection.
- ⊙ Hypocomplementemia:-
  - ↓ C1, C3, C4
  - (+Ve) Anti C1q antibodies.
- → (±) Ass. with:-
  1. AICTDs: SLE, SS, RA
  2. HCV, HBV
  3. Serum Sickness
  4. Schnitzler Syd.
- → System manifs:-
  - ⊙ Angioedema
  - ⊙ COPD
  - ⊙ Arthritis
  - ⊙ Uveitis
  - ⊙ GN.

Arthralgia
Abd pain
Uveitis
low grade fever
GN

NB: ↓ aggressive therapy

- → Schnitzler's Synd.:
  - UV + Monoclonal IgM gammopathy + ≥2 of the following:
    - Fever
    - L.N
    - Arthritis
    - boneache
    - HSM
    - ↑ ESR
    - ↑ WBCs

UV
↳ IgM gammopathy
+ (2) NL

- Fever
- LN
- HSM
- ↑ESR
- ↑ WBCs
- Arthritis
- Boneache

# 3. Henoch-Schonlein Purpura (HSP)

IgA

## (Anaphylactoid purpura)

- **Def.** Type of (SVV) That Typically affects children (<10 Ys) following (R.T) inf.

- **Incid.**
  - ⊙ Commonest Type of Vasculitis affecting children.
  - ⊙ **Age**: Typically [4-8 Ys] but adults may be affected. · **Sex**: [Boys > Girls.
  - ⊙ **Season**: More in [Winter]

- **Pathogenesis**: → Immune Complex deposit. DIF: IgA + C3 Fib.

- **C/P**: Boy (4-8 Ys) → URTI (strept / viral) → 2 Ws →

Tetrad of: **P A P A H**

**(100%) Purpura** (P)
- at Lower extremities & buttocks (النمط القحافي)
- resolve ∈ in [6-16 Ws] but recurrence ± occur (5-16%)

**Abdominal Pain** (90%)
- Simulating Acute abd.
- Paralytic ileus & intussucept. may occur.

**Arthralgia & Arthritis** (60%)
- of ankle,
- Knee
- L.L Edema

**Hematuria** (40%)
(Renal involvement) ↓ 4%
- usually mild (Mic. Hematuria & minimal proteinuria)
- Self limiting
- only 2% will → RF (2%) show renal impairment (Hafold risk > N.S)

Scrotal Edema (2-3%) → Doppler to DD Torsion

**Renal affect.** may occurs after appearance of Rash by ≃ [3 ms] (كلشان كده متابعة البول لفحص لده ٢ شهور)

⊙ **Renal affect.** in **Adults** more common أشد، specially if:
1. Fever
2. ESR
3. Rash above the waist. [فوق الوسط]

poor prognostic factor:-

1- RF at time of onset
2- Nephrotic synd
3- HTN
4- ↓ Factor XIII activity

HSP

| 1-ACR: ≥ 2 Criteria | 2- European League Against Rheumatism (EULAR), 2006 |
|---|---|
| ACR 1990<br>1- Palpable purpura (3P)<br>2- onset ≤ 20y<br>3- Abd pain<br>4- H/p: granulocyte in small bl-vs | TABLE 1<br>European League Against Rheumatism and Paediatric Rheumatology European Society Criteria for Vasculitis<br>★ Mandatory criteria<br>✓ Palpable purpura (3P) 1<br>★ Plus at least one of the following criteria ≥ 1<br>+ Diffuse abdominal pain<br>+ Immunoglobulin A deposition in any biopsy (IgA) → in Biops<br>+ Arthritis/arthralgias<br>+ Renal involvement (hematuria and/or proteinuria)<br>Adapted from [illegible] |

PAPAH
+ IgA

IgA vasculities:-

- HSp
- mixed cryoglobulinemia
- Rh Vs
- Livedoid Vs

- Pathology & DIF: ( ↑ preserved Morphology. الأنسجة سليمة )

LCV ← + leukocytoclasia
dermis [ (Nuclear dust) (Neutrophilic degranulation / fragmentation)

"predominance of "IgA" + C3 (في جدار الأوعية) within bl.vs wall
وقد C3 ↑ fibrin

- Invs: → تحاليل الالتهابات ..

1- ESR سرعة ترسيب ✓

2- تحليل بول وبراز
urine [ Mac. & Mic. (دم) Hematuria & Proteinuria.
Stool
for

3- قياس الضغط Bp ✓

US → أفضل طريقة لتشخيص الانغلاف (Ileocolic)

Biopsy ← P AP A H
- ESR
- Urine, BUN
- BP
- Barium enema
- US
- Stool

لكن ... الأفضل تشخيص (3) القرحة

4- أشعة بالصبغة على الأمعاء
Barium enema / US
"Spiking or Cobble stone appearance of intestine"

5- Skin Biopsy = عينة جلد ✓

Criteria of Dx:-
1. ACR الجدول
2. CHCC Criteria:
LCV + IgA ← deposits.

4 عدد
1+1 3 بقع

Treatment
(mainly supportive)

P (Purpura) → Dapsone, Colchicine

AP (Abd. Pain) → - NSAIDs. - H2 Blockers. - Cs (Effective > analgesics)

A (Arthralgia)

H → Hematuria & Nephritis
→ use of Cs or other Immune Suppressives in ↑↑ or Prevention is Controversy
→ arrest Progressive GN.

also IVG indicated if:
- resistant purpura
- persistent Abd. pain.

# 4- Acute Hemorrhagic Edema of Infancy (AHEI)

(Finkelstein's dis = Infantile postinfectious Iris like Purpura & Edema)

ترجع خلال ٢ أسابيع ← Edema FAHM ~٦, Targetoid purpura حميد ← ABs & URTI عنده عيل سنين

ch' BY

* Age < 2Ys (4 ms - 24 ms)

* Recent history of:

HX
- URTI (staph, strept, Adeno أو أشهر)
- Antibiotics

* Lesions: Abrupt onset of Cockade, annular or Targetoid purpuric lesions involving:

Acral
- Face
- Ears
- Extremities

Then spreads proximally to involve scrotum & Trunk

* Ass. with: Scrotal / Acral Edema & (+) FAHM.

Torsion لازم أفرق

ملخص (مهم)

<2Ys, URTI (or) Antibiotics → Abrupt & Targetoid annular purpuric lesions; firstly Acral then proximally ass. ē Edema (Acral / Scrotal) & FAHM → 1-3 ws → Spont. Resolution

تشخيص

* Fate → Spontaneous recovery within 1-3 Ws. Without Sequele.

DD: HSP
- EM
- Kawasaki
- Meningococcemia

تشابه: Similarity
- following URTI
- favors ♂
- seasonal (شتاء)

اختلاف: X but AHEI differs in:
- Younger Age (<2y)
- Resolve quickly
- Lacks IgA on DIF
- Rarely ass ē systemic sympt.

* Tt:
- 1st line → supportive
- 2nd " → anti Histamines
- 3rd " → Cs

تشبه Gottron Papule of RA

diurnal variation

# 5- Erythema Elevatum Diutinum (EED)

(Chr- Fibrosing LCV). (updated 2012)

C/P → Multiple, Bilat, Symmetrical → Papules, Nodules & Plaque ± ulcers & Blisters — Ch By:-

① - Violaceous, red-brown or yellowish

② - Early: Soft, Later → Hard → fibrosis

③ - Site: over joints of Hands, feet, Knees, Elbows, palmar Eminences, buttocks, Tendon Achillis (Pressure Areas) ✓

(✗ → Sparing the Trunk) ✗✗

Etiopathog (Triggers)

- Inf ← Bact: Strept / Viral: HBV, HIV
- Hematological Mg: (BCL) MM
- Rheumatological dis
- Ig A Gammopathy (SLE)
- GF

IL8 plays a role ✓

- Age: 30- 60 Yrs
  - ♂ older (Hutchinson Type)
  - ♀ younger (Bury Type)

④ - May show Central clearance & diurnal Variation (يزيد نهاراً وقل ليلاً)

⑤ - Common Ass: ocular affect → (اتابع)

⑥ - Very chr & persistent: resolve in 5- 10 Ys (but may last upto 40 Ys)

⑦ ± → Atrophic scars.

- Pathology ① Early cases: → LCV (الكتب عن) — Dif ← C IgG IgA IgM

② Late Cases (Sclerosis) → عشان كده لون Yellow

(لاستخدم هايبا لان في جرح في النسيج)

- Extracellular Cholesterolosis (EC) (Intra & extracell. Cholest Deposit)
- + Fibrosis (onion-like perivascular) → hard

- Treatment:
  - DapSone (الأفضل) (For: Long time)
  - IL Cs (systemic not indicated)
  - Nicotinamide
  - PLEX: intermittent plasma exchange (Severe cases) — (بديل)

Cold ↑ Igs ↑

# 6- Cryoglobulinemia.

HCV

Ig

**Def:** presence of abnormal Immunoglobulins that precipitate at cold Temperature & redissolve on rewarming (at 37 °C) e.g (presence of abnormal Cold Precipitable Igs)

Vasculopathy → (IgG + IgM + C)

Vasculitis → (Ig)

**Types of Cryoglobulinemia:** (Brouet classification):-

| Type & % | Ig Type | Immune Complex | Associat^ |
|---|---|---|---|
| Type I (10%) | Single Monoclonal IgM (less common IgG) | X None<br>Vs occlusion | ↙ Lymphoproliferative disorders:<br>• Leukemia<br>• Lymphoma<br>• MM<br>• Macroglobulinemia (Waldenstrom's) |
| Type II (60%) (mixed Type) | Monoclonal / polyclonal<br>(Monoclonal IgM ē +ve RF* against Polyclonal IgG) | Vs IgM-IgG (+ IgG-IgG or IgA-IgG) | HCV AICTDs - lymphoprolif<br>HCV (90%)<br>CTDs:<br>↙ RA (45%)<br>• SLE (25%)<br>• SS (Sjogren) (15%)<br>• Systemic sclerosis (10%) (SSc)<br>⊙ others<br>HBV (5%)<br>HIV (25%)<br>← Lymphoprolif (5%) |
| Type III (mixed Type) (30%) | Polyclonal / polyclonal<br>(Polyclonal IgM ē +Ve RF against Polyclonal IgG) | IgM-IgG (+ IgG-IgG-IgA) | |

Clinical: Raynaud's Phenomenon, Retiform purpura, gangrene, acrocyanosis, HCV, AICTDs, Lymphopx, palpable purpura, PN, arthralgia, GN

[B] RF: Rheumatoid factor activity = means that this IgM can bind to Fc portion of IgG.

HCV: is the most common cause of cryoglob.

NB - Type II & III are

- Commonest types.
→ called "Mixed Cryoglobulinemia" or "Cryoglobulinemic Vasculitis" because they cause Vasculitis but Type I don't cause Vasculitis [but Vasculopathy]

Another old classification
Type Essential (idiopathic)
(Y (d.t underlying Et.)

- Pathophysiology of Vascular damage in Cryoglob. :-

- Type I (No Immune complexes): → Vascular occlusion (d.t ppt & thrombosis) = (Vasculopathy)

- Type II & III (+ve Immune Complexes): → Vasculitis (LCV).

NB
- Median age: 60 y
- Cryoglobulins are +Ve in low titre in 50%

## CIP of Cryoglobulinemia

1- Type I (only Cut manifs; No Systemic affect (but ± renal)):
- Retiform purpura
- Acrocyanosis
- Raynaud's
- Arterial Thrombosis.
- Gangrene.
- Cold urticaria.

Mostly Acral

→ Peripheral Vascular insuff → occlusion vs nl

2. Type II & III: (Cut & Systemic) : Tetrad: PN. purpura. arthralgia. RenalDis

skin
GIT
Joint
GN
PN.

- 3P (but ± urticaria, Livedo, retiform purpura, leg ulcers)
- Arthralgias 70%.
- PN (sensory ++ & motor weakness).
- GIT dis & Hepatitis.
- G.N.

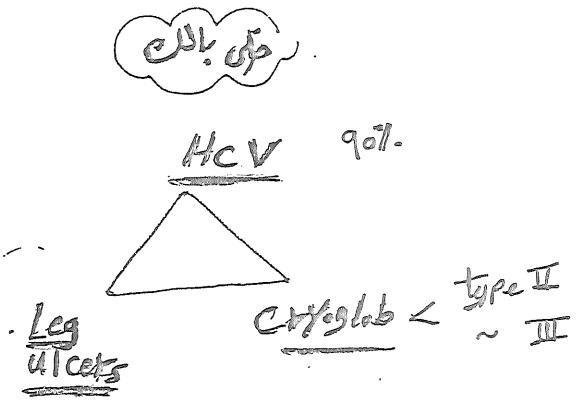
(Ulcer & purpura) around Ankel

↓

Mixed Cryoglobul

↓

HCV




- Type I → Mg = (lymphoproliferative dse)
- Type II & III → Infection & Autoimmune [AICTDs, HCV]
- IgM → RH

→ DD

- Cryoglob.
- PG
- Artefacta = (dermatitis artefacta)
- Ecthyma Gang.
- Calciphylaxis.
- Necrotizing fasciitis.

## Invs: ① Tests for Cryo-globulins :-

لو ظهرت سلبية نعيدها كذا مرة أثناء ال (( Clinical attack ))

يجب عينة الدم في أنبوبة عند درجة حرارة ٣٧°.

تسيبها يحدث ليها تجلط ثم نفل الـ Centrifugate ← Serum.

تحضن عند درجة Incubator لفترة : (4°C).

Blood sample 37 → Serum Centrifuga → Incubator 4°C (ppt)
- 24h → type I
- 7 ds → type II

Serum

- Type I → ppt within 1st 24 hrs (at conc > 5mg/ml)
- Type II → ppt at ≈ 7 ds if small sample (< 1mg/ml).

then → incubate at 37°C → redissolving.

Tt of Cryoglobulinemia :-

underlying AE
- e.g HCV 90% → IFN & Ribav.
- CS → Cyclosporine
- Rituximab / IVIG

then Cryoglobulin Conc. can be determined via Spectrophotometric analysis.

Specific Immunologic Assays may be used to identify Cryoglobulin → Components (Igs, Light chain & clonality).

## ② Histopathology & DIF :-

- * Papular lesions → LCV (SVV).
- * Ulcerative " : → Medium sized vasculitis.
- * Granular: C3, C. IgM (أكثر نوعين) at BVs.

عشان كده لبعض بيصيبها عالأغلب (small-med)

# ANCA Vasculitis

(23)

**def. of ANCA:** group of antibodies (mainly IgG) against Antigens in Cytoplasm of Neutrophils & monocytes.

**Types of ANCA:** (Acc. to their staining Pattern):

1- **C- ANCA:** (Cytoplasmic ANCA) (cp)

- Antibodies directed against Proteinase 3
  → (PR3) Ag → granular Cytoplasmic staining.

another Ags: Lactoferrin, Cathepsin G, Elastase

2- **P- ANCA:** (Perinuclear & Nuclear ANCA) (PM)

- Antibodies directed against Myeloperoxidase
  → (MPO) Ag → perinuclear staining.

3- **X or Atypical ANCA:-**

- Antibodies Neither directed against (PR3) Nor (MPO). [another Ag]
- Diffuse Cytop. & Perinuclear.

**Detection of ANCA:-**

① first → IIF if +ve do:
② ELISA (Confirmatory).

لسهولة الحفظ

- WG → C- ANCA
- CSS → P- ANCA
- MPA → Both (P ANCA > C-ANCA) (MPAN)

other dis: SLE, RA, IBD, chr. inf.

تفصيليا (HL)

- WG < 80% C-ANCA, 10 P- ANCA
- CSS < 60% P-ANCA, 10% C ANCA
- MPA < 60% P-ANCA, 30% C ANCA.

Vasculopathy:

- ✓ Vs wall infiltr.
- ✓ fibrin deposition & Thrombosis

No ✗ inflammation, infiltrate, destruct

CSS phases

A) 1st: Allergic Rhinitis, Asthma, Nasal Polyps, Periph. Eosinophilia

الأنف

B) 2nd: Vasculitis

C) 3rd: Allergic Rhinitis, Asthma, PN, HTN, Resolut. to other systems

# Wegener's Granulomatosis (45ys)

- Definition: syndrome consisting of Necrotizing granuloma of (RT (upper&lower) → otitis, Epistaxis, saddle, sinusitis; Kidney → Necrotizing GN; BVs → " Angitis)
- CIP → ROUGH + Cut.
- ACR Criteria for ⊕: (≥ 2)

Wegener's granulomatosis (WG)
1. Nasal or oral inflammation
2. Chest X-ray showing nodules, infiltrates (fixed) or cavities
3. Microscopic hematuria or red cell casts in urine
4. Granulomatous inflammation on biopsy (within vessel wall or perivascular)

Two criteria classify WG with a sensitivity of 88.2% and specificity of 92.0%

- Pathogenesis: (HL)
  - genetic PR3 (proteinase) polymorphism
  - Staph. nasal infection
- Biopsy ? (بيوبسي) → Vs + Granulo.
- Manifs → ROUGH
  - Radiographic Abnormalities of CXR (Nodules-Cavities-infilt).
  - Nasal & oral ulcers
  - Urinary Sediment (RBCs, casts, Hematuria.)
  - Granulomas of lung/skin
  - Hemoptysis.
  - others: Cough, Dyspnea, chest pain.
- Tt: CS + Cyclph. / CS + MTX / Rituximab. / Septrin (↓ relapse L Inf.)
- Ut. manifs (40%)
  - LCV
  - urticaria
  - Purpura
  - petechae
  - PG.
  - Papulo-Necrotic lesions at Elbows → ulcerat.
  - Gingiva: red, friable, Hyperplastic (IPSS) (Pathognomic)

## Churg strauss Synd (CSS). (♀, 35ys)

(Allergic granulomatosis or Angiitis).

CIP: (6)
- Asthma
- Eosinophilia
- sinus Abnormality
- PeN
- Pulm. infilt.
- Perivascular Eosinophils on Biopsy. (eg)

ACR Criteria (≥ 4 → diagnostic) ⊕

- Cut. (55%): → ++ (P: Purpura (++), S.C Nodules (+))
- others ± Granuloma
  - Path: Eosinophilia, Extravascular granulomas, Necrotizing vasal ± small med sized.
  - Purpura, Nods
  - Papulo necrotic lesion: Eos. abscess, palisaded Eos. dermatitis

Commonest cause of death:- MyoCarditis & HF

Other manifs: CNS, CVS, MSK, ocular, cut. (↓↓)

→ May be drug induced:-
- Azithromycin
- HBV Vaccine
- Zafirlukast

Ecs. Cationic protein.

HL

## Differentiate bet. WG & CSS

(1) granuloma (3) Asthma Eosinophilia Granuloma.

| | Wegeners | Churg Strauss |
|---|---|---|
| (E) Asthma | – | + |
| (E) Eosinophilia in Blood | – | + |
| (E) perivascular Eosinophils on Biopsy | – | + |
| (2H) Hemoptysis | + | – |
| (2H) Hematuria | + | – |
| . C-ANCA | 80% | 10 |
| . P-ANCA | 10% | 60% |

E = عيزة عنزة

## Microscopic polyangiitis (MPA)

Commonest ANCA type
- No granuloma
- No Asthma
- Kidney is the most Commonest

Dermo pulmonary renal Synd.

✓ Commonest ANCA Associated Vasculitis

✓ Commonest organ affected is: Kidney

~50 Ys
M > F

. CIP .
- fever
- Arthralgia
- Myalgia

→ may appear ms- Ys before Explosive phase of the dis.

Most Common ← Type ANCA & organ Kidney

O
X
- No Asthma
- No Eosinophilia
- No Granuloma

Δ
- Neuropathy.
- G.N (RPGN 80%, → Necrotizing GN)
- pulm. involvement & Hge.

. skin manifs : purpura, Erythema & urticaria, Nodules, Ulcers & splinter Hge.

. ANCA = P-ANCA (60%) > C-ANCA (30%)

GN
PN — pulm

HH Cs, Cyclophosph, others.

De

# Medium Sized Vasculitis (2016)

A- PAN → HBV

B- Kawasaki

---

## A PAN (Polyarteritis Nodosa)

- Def: Necrotizing Vasculitis affecting Small-Medium sized arteries Commonly: Segmental

of branching points

- Coronary
- Hepatic
- Renal
- Cut.

→ Clinically at their branching points.

→ Aneurysmal dilatation (or)

- Age: ~40-60 ys. Children.
- Sex: M > F 4:1
- Association: classical associations:

(classic) → Systemic Type → HBV (or)

(Bg) → Cut Type → silent inf.; ↓HBV !? → HIV

Other ass. (2 types.)
- FMF
- SLE
- IBD

- Treatment
  - ↓ of inf.
  - stop the drug
  - NSAIDs
  - Cs + Cyclo / Mtoph + Azathio
  - MTX
  - Dapsone
  - other Immunosuppressive drugs.

Types: 1- Bg Cut. (10%)

"classical Type" → 2- Systemic. (affect muscular a.a of vital organs).

- CIP: A. Systemic Type (90%)

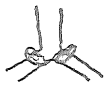
* systemic Manifs: FAHM myalgia, Wt loss, fever, N-sweat
  - Mononeuritis Multiplex
  - CHF
  - Renal: HTN & RF.

* Cut manifs (50%): → usually Livedo reticularis & (LR) Nodules & Punched out ulcers

(B) Cutaneous Type (10%)

- More in children (BA) ~U
- mild & self limiting
- usually affects the L.L: Livedo Retic. / painfull S.C Nodules & punched out ulcers -

Histopathology: Segmental Necrotizing Vasculitis at branching points → Aneurysmal dilatation.



ACR for diagnosis: (3/10)

- Wt loss > 4 kg
- Livedo Retic.
- Pain: Testicular pain / Ms or leg pain
- HTN
- PN
- lab: ↑ BUN (or) ↑ S. Creat.
- +Ve (HBV)
- +Ve Arteriogram → Aneurysm or occlusion.
- +Ve Biopsy.

Rx:

1. HBV: Best → IFN α + Vidarabine
2. Cs ± Cyclophosphamide.
3. Rituximab (or) IVIG.

~~DD~~ → EN

MC LN syn

## Kawasaki Disease (Mucocutaneous LN syndrome)

**Def:** Type of medium sized vasculitis characterized by Coronary vasculitis with non specific cutaneous manifestations

**Etiopathogenesis:** ?? 1-Genetic, 2-Autoimmune, 3-Toxin-Mediated Super Ag ← strept, parvovirus 19

### Kawasaki Disease Diagnosis Criteria

knowmedge

*Mnemonic: "CREAM"*

**Criteria**

Fever >5 days

Fever for ≥5 days → >38°C, Not responding To Antibiotics

+

4 out of 5 of the following

| | |
|---|---|
| C | Conjunctivitis (non-exudative) |
| R | Rash (polymorphous non-vesicular) → Specially (Perineal) (May be early Manifs) → easily desquamate |
| E | Edema (or erythema of hands or feet) |
| A | Adenopathy (cervical, often unilateral) |
| M | Mucosal involvement (erythema or fissures or crusting) strawberry tongue |

Fever + CREAM



### Methods- Classification

**Complete KD:**

- 4 clinical signs (CREAM)
- Fever for at least 5 days

**Incomplete KD:**

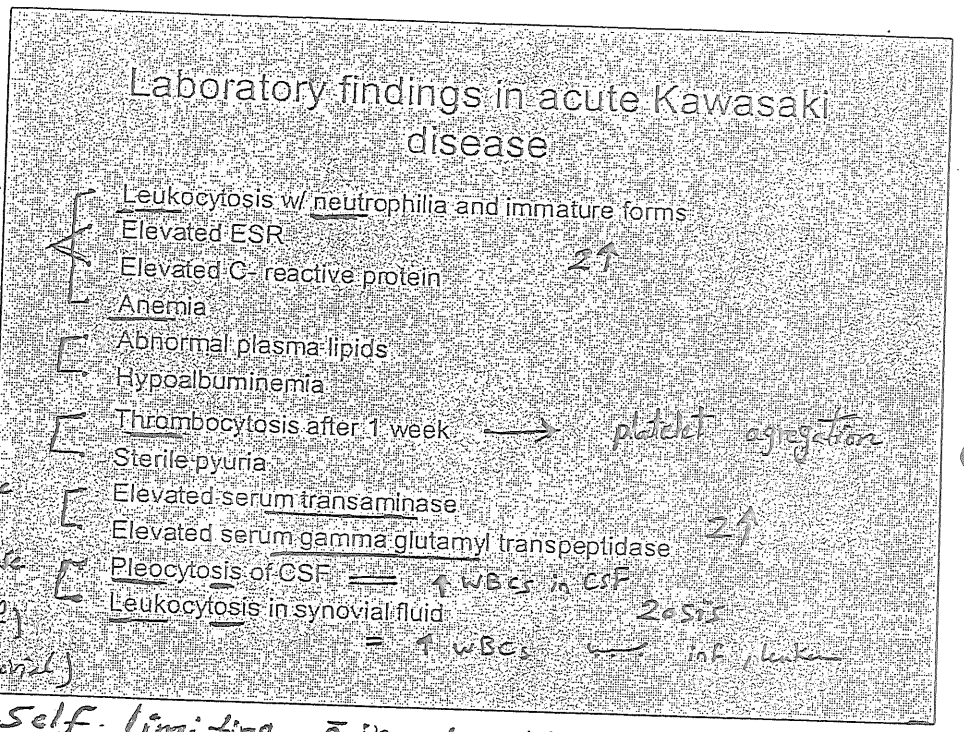
- 2 or 3 clinical signs
- Fever

All patients received standardised treatment and follow up → c/o أخلاف قسم الـ

- **Clinical:** Criteria & BCG scar reactivation/inflammation ← مهم جداً
- **Two-dimensional ECHO** or **coronary angiography**
- **Lab.**

القلب مكان تطعيم BCG

NB cut. HP → Non specific Pathology.




1- CBC ← L, N, A

2 ↑ ESR, CRP

plasma lipid ↓ albuminemia

sterile pyuria

3 ↑ Sr. Transaminase, γ glutamyl transpeptidase

pleocyt (CSF)

leukocyt (synovial)

Anemia, leukocytosis, neutrophil

CBC

↑ ESR

↑ CRP

↑ Sr. transaminase

↑ Sr. γ glutamyl tr. peptidas

↓ Albuminemia

plasma lipid [Ab

pleocytosis [CS

leukocytosis [Syno

Thrombocytosis

sterile pyuria

= urine analys

- Self. limiting ē in 1-3 Ws
- 25% → Coronary aneurysm → Thrombosis & MI (MR 2%)
- NB - Rash + fever لازم تتوقعي أي حالة
  - become the Most common Acquired Heart dis in children after Rheum. fever.

DD:
- SSSS
- TSS
- Exanthema
- EM & DE.

---

[##]

① Aspirin (Thrombus ضد)

80-100 mg/kg

تقسم على 4 جرعات يوميا طيلة فترة الحمى

أو بعد يومين من نزول الحرارة

↓

Maintenance 4 mg/kg/d

For 6-8 Ws.

بديل لأي شخص عنده أطفال

(Clopidogrel) ← ١ سنة

+

② IVG (Aneurysm ضد)

تعطى مرة واحدة فقط

↓

2gm/kg/12hrs

تعطى وريدي على مدار ١٢ ساعة

Alternative to IVIG:

- Pulse MPA (Cs)
- Infliximab
- Ulinastatin (protease inhibitor)

# Large Vs Vasculitis

(31)

## • Giant (Temporal) Cell arteritis [Horton's dis]

>50y

- Def: granulomatous Vasculitis of Aorta, its Major brs & Medium sized Vs. Specially Extra-Cranial brs. of Carotid the Temporal a. (Head & Neck) (specially)
- pt >50Ys (♀>♂)
- Etiopath: IFN-γ (by T cells) → ++ Multinucleated giant cells & Macrophages → factors → myofibroblast prolif. → Intimal Hyperplasia → arterial lumen occlusion
- C/P 1- systemic: Headache, Earache, Sore throat, Jaw Claudication
  - ← Blindness.
  - ← Pain & stiffness of Pelvic & shoulder girdle
- 2- Cut (rare) = Tender, Nodular, swollen, Indurated, pulseless Temporal artery.
- Tt (Cs) ± (MTx)

## • Takayasu arteritis

<50y

- Granulomatous Vasculitis of aorta & Major brs that affect pt <50Ys
- (Aortic Arch Synd = pulseless dis.)
- Etiology: Inf: TB & Viral; Genetic; Autoimmune
- C/P
  1. pre-pulseless phase: fever, wt loss, arthralgia (← wt loss, Fever, Arthralgia)
  2. Pulseless phase:
     - Bruit, No pulse ←
     - ← Irregularity of Bl Pr at arms & legs.
     - ← HTN, Headache, Angina, Seizures,
     - ← Retinopathy
  3. skin lesions
     - (Early): EN & EI like
     - (Lat): PG like
- HP of skin:
  1 - Granulomatous Vasculitis
  2 - lobular & septal panniculitis +
  3 - Fat Necrosis.

# Vasculopathy

1- Degos dis.

2- Erythromelalgia.

(Chr. of vasculopathy:-)

i. Fibrin deposit or thrombosis ± acut vascular inflamm.

ii. Vs wall infilt. ± alterat.

iii. ± other features.

## 1- Degos dis (Malignant Atrophic papulosis)

**Def** Autoimmune Vasculopathy causing occlusion of Small & Medium sized arteries in 4 systems ← skin, GIT, CNS, Eye → ischemia

**Etiopathogenesis:** unknown ± d.t

1. Genetic: ?? AD
2. Autoimmunity
3. Viral inf.
4. disturbed clotting system.

→ All (±) → ↓ Endothelial defect ± Impaired platelet + Fibrino lytic activity & C5

**Hematological / Endothelial / Clotting dis. ± C5 defect**

[Not considered Vasculitis as there is no arterial wall injury & No Immune Complexes]

**Epidemiology:** Age: Young adults.

Sex: M>F (3:1)

**Clp** (1) Cut lesions [precede the systemic lesions by yrs]

- 30-40 Asympt, Small sized (2.5mm) dome-shaped papules → become Necrotic & Umbilicated → heal ± porcelain White scars surrounded by Telangiect.
- Site: Mainly at trunk [back] & limbs.

2 forms: By cut, systemic

2- GIT lesions: → Acute abd pain, Bleeding, perforation → death. [Cause of death] [5% in 5 Ys] (33)

3- Nervous lesions (CNS): stroke, Headache, Epilepsy, ...

4- Eye: diplopia & visual defects.

---

Path → Epid: Atrophic ± some hyperkeratosis
Dermis: Wedge shaped alteration (Edema, mucin, sclerosis & Necrosis)
Vascular: damage & Thrombosis

Tt: ① Cut. lesions:
- Antiplatelets ↔ Aspirin / Dipyridamole
- IVIG

② systemic dis: → Eculizumab (approved for PNH) [anti C5 (--- its activation)]
(PAH) Treprostinil ( " " pulm HTN)

DD: Dego's like in AICTDs & APLS.
LSEA.

↓
→ Guttate Morphea
→ Lichen sclerosis et Atrophicus

# Erythramelalgia (Erythromalgia)

- Erythro = redness
- Melos = Limb
- Algos = Pain

(34)

- **Def.** Episodic attack of: Hotness, redness, burning sensation at palms & soles that ppt. by warmth & hanging down & ↓↓ by Cooling & limb Elevation. → at night

- **Etiopathogenesis:** → unknown; there are 2 Types.

  - I: Thrombosy
  - II: 1ry
  - III: asse other than thrombo.

**1ry (Idiopathic)**

- Genetic Mutation in Voltage-gated (Nat) channel → ↓ threshold & ↑ hyper Excitability of Pain Neurons.

**2ry**

A — Thrombocythemia ass. (platelet show ↑ No & dysf → Microthrombi)

B — Non thrombocythemia ass. → ± asse

- Myeloprolif disorders
- DM (Diabetes)
- PVD = peripheral Vascul dse
- Vasculitis
- AICTDs (SLE)

---

- **Epidemiology:** Age: childhood - Adulthood
  Sex: F > M.

- **Clp** مع لسعة أو نزلة برد بعد (٣) سنوات - حرقان - احمرار
  غالبا في القدم (٩٠٪) أو في اليد (٢٥٪) يجي فجأة بالليل (يكون محتمل يبقى مستمر)
  وتفضل طول الليل ومكنه يصحيها من النوم. يخف مع البرودة أو رفع القدم والليد

- **NB** ∴ Dig (thrombocyt.): ± unilat & ± → ischaemia. نقوى

- **Exacerbating factors:** ① ↑ temp. ② hanging down ③ Walking or standing

- Path: XT → Biopsy (not) required & Non specific.

1- chr. regional pain synd (reflex sympathetic dystrophy & causalgia)

- Autonomic dysreg.
- AEt ??
- Pht: injury surgery

نفس أعراض وكأنها: بقعة مستمرة
وليس لها علاقة بدرجة الحرارة.

2- P.N: may Cause Tingling & Numbness (ت) diff → Nerve Conduct study)

3- CCB & PV occlusive dis. (PVD)

NB → لازم نخلي بالك من المرضى لأنه معرضة لـ Myeloprolif. dis

## Treatment (علاج)

1- General: ارفع رجليك وبيك + تبريد الأطراف [Cooling, leg elevation]

2- Thrombocythemic ass. type → aspirin

3- Other Lines:-

- SSRI.
- Gabapentin.
- CCB
- Tryptizol
- Capsiacin (lot) (↓ pain)
- Nitroprusside
- PGE,
- Lidocaine
- opiates
- Epidural anaesthia

# Livedo Reticularis

Mild — physiological

Def: Reticulated vascular pattern ⓦ usually representing ↑ vaso-spastic response to cold (but ± dft underlying systemic dis. (3C)

| CAUSES OF LIVEDO RETICULARIS | |
|---|---|
| Congenital livedo reticularis | |
| ✓ Cutis marmorata telangiectatica congenita (Vascular Malformat-) CMTC | |
| Acquired livedo reticularis | |
| (1) *Vasospasm* (Most Common Cause):- (VC)<br>• Cutis marmorata/physiologic livedo reticularis<br>• Primary (idiopathic) livedo reticularis<br>• Autoimmune connective tissue diseases (e.g. SLE)<br>• Raynaud's phenomenon/disease | • Idiopathic (1ry) = cold<br>• physiologic (CM)<br>• AICTD.<br>• Rayn. |
| (2) *Intravascular/reduced flow*<br>⊙ Increased normal blood components : (↓ Bl. flow) ↑ Coagul, ↑ Bl. Compact, Abn prot<br>[ Thrombocythemia<br>Polycythemia vera<br>TTP<br>⊙ Abnormal proteins :<br>[ Cryoglobulinemia<br>Cryofibrinogenemia<br>[ Cold agglutinins<br>Paraproteinemia<br>⊙ Hypercoagulability :<br>– Antiphospholipid syndrome ✓ APS<br>– Protein S and C deficiencies<br>– Antithrombin III deficiency<br>– Factor V Leiden mutation<br>– Homocystinuria, hyperhomocysteinemia<br>– Disseminated intravascular coagulation (DIC)<br>⊙ Thrombotic thrombocytopenic purpura | [ thrombocyth.<br>PCV<br>[ APS.<br>DIC<br>[ Cryoglob.<br>Cryofib.<br>[ protein S & C<br>para proteinemia |
| (3) *Vessel wall pathology* (Vasculitis / Livedoid) (calciphyl. / Sneddon's) (4) | |
| ⊙ Vasculitis (Medium sized) ← PAN, Cryglob.<br>[ Cutaneous polyarteritis nodosa<br>Systemic polyarteritis nodosa | |

(4)
- Vasculitis — CM, Wap, Med
- Sneddon's Syn
- Calciphylaxis
- Livedoid vasculopathy

## CAUSES OF LIVEDO RETICULARIS

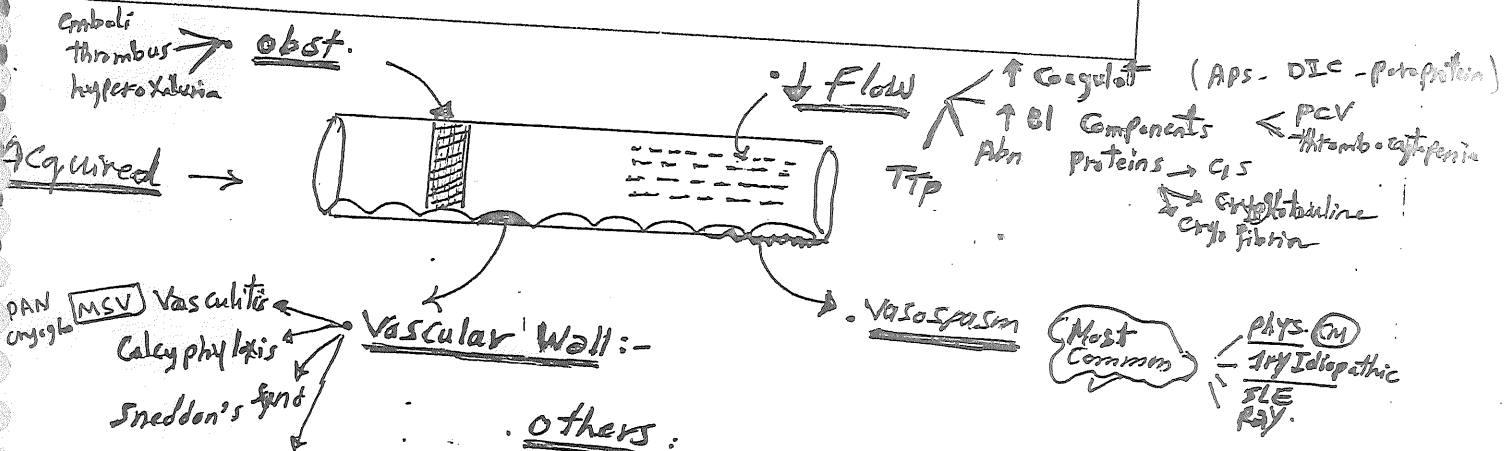
- Cryoglobulinemic vasculitis
- Autoimmune connective tissue disease-associated vasculitis (e.g. rheumatoid arthritis, SLE, Sjögren's syndrome)
- Calciphylaxis
- Sneddon's syndrome
- Livedoid vasculopathy (also intraluminal obstruction)

*Vessel obstruction*

- Embolic
  - Cholesterol emboli
  - Septic emboli
  - Atrial myxoma
  - Nitrogen (decompression sickness)
  - Carbon dioxide arteriography
- Thrombosis (see above)
- Hyperoxaluria

*Other*

- Medications (e.g. amantadine, norepinephrine, interferon)
- Infections (e.g. hepatitis C [vasculitis], *Mycoplasma* [cold agglutinins], syphilis)
- Neoplasms (e.g. pheochromocytoma)
- Neurologic disorders (e.g. reflex sympathetic dystrophy, paralysis)
- Moyamoya disease




- Others:
  - Drugs → IFN, Amantadine
  - Inf → HCV & S
  - Neopl. → pheochromocytoma.
  - Neurolog → paralysis.
  - Moya Moya dse

(CMTC) ← Cong

Large Branching

**Types**

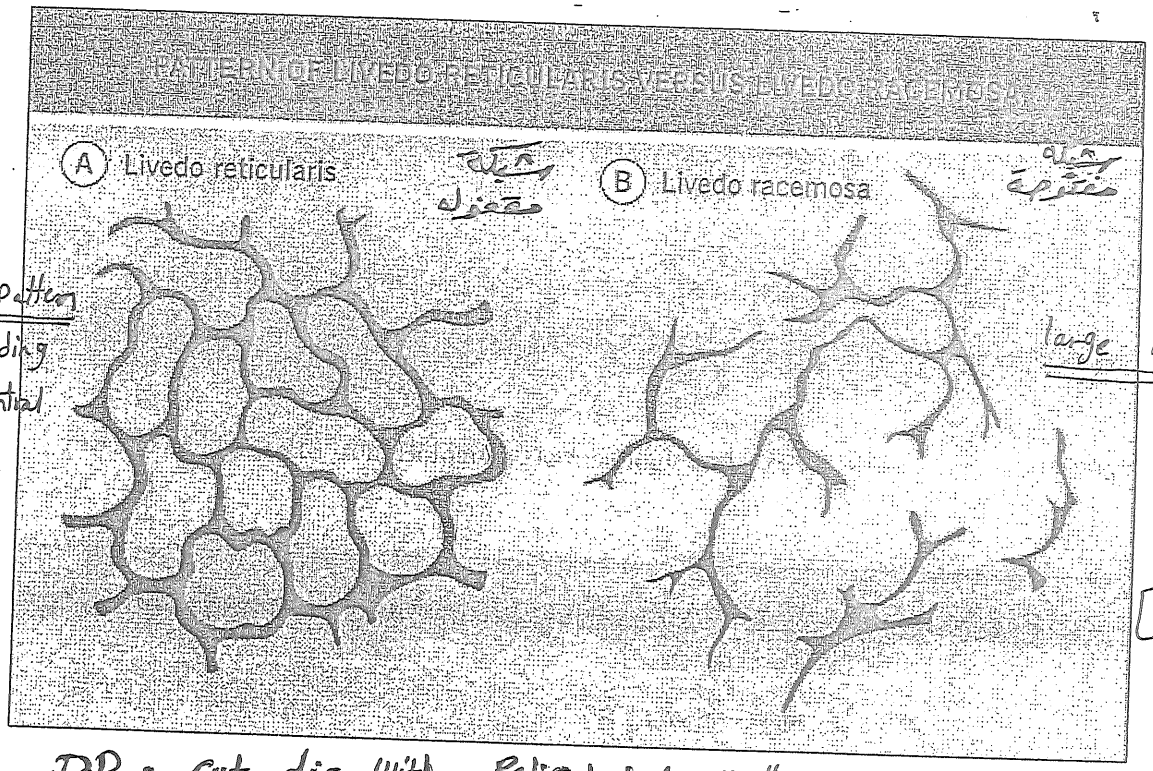
- Physiological LR: Transient (يختفي مع البرودة)
- Other causes of LR: → persistent

① **Livedo Reticularis :-**

Cyanotic (reddish-blue) cut. discolorat~ surrounding Pale Central area.

② **Livedo Racemosa :** distinct pattern of LR consisting of large branching pattern that usually occurs on Trunk & Proximal limbs.

- Most Common Cause: Sneddon's synd but ± Caused by: APS




closed pattern surrounding pale central area

large branching pattern [opened]

[ APS
[ Sneddon's

- DD : Cut. dis with Reticulated Pattern:-

1- **Erythema ab Igne :**
   - a- reversible LR like (then)
   - b- fixed reticulated hyperpigmentat~
2. **REM synd** (Favors central trunk)
3. **Erythema infectiosum**
4. **Porkeladerma**
5. **MF**
6. **GVHD**

→ Epidermal changes on pathology

# Livedoid Vasculopathy

(Livedoid vasculitis, Atrophie blanche, Livedo reticularis with summer ulceration, Segmental hyalinizing vasculitis)

- Def: Chr. Vascular disorder ch BY (2) stages
  1- Persistent painful ulcers of Lower Legs. Healing
  2- Atrophie blanche scars
- Etiopath. (Types) : 2
  1- Idiopathic (1ry)
  2- 2ry Type: Thrombosis (Coagulopathy ← platelet fibrinolytic protein defect) ? Chr. Venous insuff & Venous HTN, VV, (APS), SLE.

C/P: 2 components:

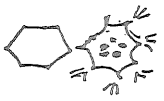
(1) ulcer: Painful, punched-out on A back ground of Retiform purpura or Livedo Retic. (Also Named) (Livedoid vasculitis) around Malleoli

(2) Atrophie blanche scar: which is characterised by:

ⓐ Star-shaped or polyangular, ivory white depressed atrophic plaques

ⓐ Prominent red dots within the scar due to enlarged capillary blood vessels

ⓑ Surrounding pigmentation. or Telangiect.



**Pathology:** The characteristic histologic findings in livedoid vasculopathy are mild perivascular lymphocytic infiltrates and extravasated red cells surrounding superficial dermal vessels with hyalinized walls and luminal fibrin deposition. ext. RBCs

Differential diagnosis

**DD:** 1- Other causes inflammatory retiform purpura (see Ch. 23).

2- Other causes Atrophie blanche: Atrophie blanche-like lesions are not specific for this syndrome, so that a history of the characteristic ulcers should be used to distinguish this form of skin injury from other disorders that can lead to atrophic scarring, *such as* APS, CSVV, sickle cell anemia, hydroxyurea-related leg ulcers, Diabetic vascular disease, Any injury to the skin of an ageing lower leg, such as following cryotherapy or curettage and cautery in the treatment of skin cancers, and **especially** venous stasis with varicosities

APS
CSVV
SCA
D.M
Injury ← Cryo, Cautry, Curettage

**Treatment :**

1. * Antiplatelet, anticoagulant and fibrinolytic therapies[53]. (Aspirin)
2. * Anabolic agents such as danazol and stanozolol.
3. * PUVA therapy[55].

* In patients with atrophie blanche-like lesions and lupus (SLE) antimalarial drugs may be helpful.
*Patients on hydroxyurea with atrophie blanche-like lesions may need a trial off the drug, since hydroxyurea may mimic this syndrome through unknown mechanisms.

# Pigmented Purpuric Dermatoses
## *(capillaritis; purpura progressive pigmentosa)*

*(Jan 2010)*

**Def:** Group of chronic diseases of unknown etiology characterized clinically by petechial hemorrhage and histopathologically by lymphocytic capillaritis. They are not associated with any systemic findings.

**Etilogy and Pathophysiology:** The etiology is unknown. However the following may play a role:

* Venous hypertension
* Gravitational dependency
* Exercise
* Genetic predisposition *(familial cases of Schamberg disease and Majocchi disease have been reported).*
* Drug.

They are not associated with any systemic findings or coagulopathies.

**Epidemiology:** -Age: * Schamberg → any age.

* Majocchi and Lichen aureus → children or young adults.
* Eczematidlike purpura and the pigmented purpuric lichenoid dermatosis → middle-aged men (40-60).

- Sex: All (M > F) except Majocchi (F>M).

-Race: no predilection.

**C/P:** -There are 5 classical types:

1- Schamberg's disease *(progressive pigmentary dermatosis).*
2- Majocchi's disease *(Purpura annularis telangiectodes).*
3- Pigmented purpuric lichenoid dermatitis of Gougerot and Blum.
4- Eczematid-like purpura of Doucas and Kapetanakis *(itching purpura)*
5- Lichen aureus *(lichen purpuricus).*
6- Other rare types: (A) Granulomatous, (B) Familial, (C) Linear and quadrantic

→ Pigmented purpuric Erupt

(44)

NB: Many consider itching purpura and eczematidlike purpura to be variants of Schamberg disease

* Clinical features: All cases Ch. By: الأعراض الأكثر

→ Orange-brown, speckled, cayenne pepper–like discoloration (due to hemosiderin deposition)

→ Usually affect lower legs and ankles, however any site can be affected even the face and palmoplantar. (L.L) غالباً

→ Usually asyptomatic except itchy purpura which shows severe itching

→ Have very chronic course.

1-Schamberg's disease: any age / ♂

- Most common type.

- Lesion: *patches or Plaques:* red – brown with pinpoint 'cayenne pepper' macules (represent petechiae) usually bilateral at lower legs and ankles but can also occur on the thighs, buttocks, trunk and arms (however) a unilateral distribution is occasionally observed. Over time, the lesions become darker brown in color and then fade, but new crops often subsequently appear.

غالباً bilat patches (Red brown) → dark brown → fades → (Recurrence)

child ♂

2- Majocchi disease or Purpura: *Annular Plaques*: 1–3 cm in diameter with punctate telangiectasias and cayenne pepper petechiae in the border.

petechia + Telangectasia

NB: A variant termed purpura telangiectatica arciformis (Touraine) consists of fewer, larger and irregularly arciform lesions. جاوجيرون

Middle age ♂ ← ch

3- Pigmented purpuric lichenoid dermatitis of Gougerot and Blum: (rare): Lesions similar to those of Schamberg's disease but there is characteristic purpuric red-brown lichenoid papules and can involve UL and LL.

Middle age ♂

4- - Eczematid-like purpura of Doucas and Kapetanakis *(itching purpura)*: similar to Schamberg's disease but differs in: (Rapid - Extensive - itchy)

كمان

* Persistent intense itching
* More extensive
* Develops more rapidly.

- ~~Lesions: scaly petechial or purpuric macules, papules and patches often with a~~
- DD: 1-Carbromal sensitivity, and less commonly with other drugs such as meprobamate, carbamazepine and perhaps even some foods.

2-Clothing or rubber dermatitis may produce a similar picture.

child ♂

5- Lichen aureus *(lichen purpuricus)*: Ch. By:

- More localized
- More intensely purpuric

ē Hemosiderin from RBCs extrav.

Def. Clusters of petechial Age ē chr. Hp of.

(1) Schamberg: patches & plaques - red-brown ē cayenne pepper-like dots (petichae) → Fade ē dark brown Colors → exacerbat∩ remission.
(2) Majocchi → annular plaques ē Petichae & punctate Telangiect
(3) L. Aureus → solitary, chr. plaque ē rusty Color ± surrounded by orange-hue.
(4) Itching P. → as Schamberg but Rapid, extensive & itchy

(42)

Rust = golden

- Lesion: solitary, chronic patch or plaque with rust to purple-brown color but may have a golden hue.

6- Other rare types:

A- **Granulomatous/pigmented purpuric dermatosis** : An uncommon variant of pigmented purpuric dermatosis has been reported in which there is granulomatous histology.

B- **Familial/pigmented purpuric eruption:** rare AD familial inheritance in some cases of Schamberg and Majocchi . Discrete reddish-brown spots develop in childhood or adolescence but of larger size than in Schamberg's disease and are arranged in a mosaic pattern. The lesions gradually cover a larger area and involve new sites, mainly on the limbs and in the larger flexures, but there are no symptoms.

C- **Linear and quadrantic pigmented purpuric dermatoses** : Various morphological types of pigmented purpuric eruption may occur in a linear or zosteriform distribution , or less commonly may diffusely involve a single quadrant of the body.

**Investigations:** thrombocytopenia and vasculitis should be excluded because of the purpuric (usually petechial) nature of the lesions and clinical misdiagnosis:

1- CBC, coagulation profile, Hess test for capillary fragility.
2-Histopathology: in all cases there are Capillaritis:
1- RBCs extravasation,
2- Endothelial cell swelling,
3- Perivascular infiltrate of lymphocytes and macrophages is centered on the superficial small blood vessels.
4- Hemosiderin-containing macrophages.
5- Mild epidermal spongiosis and exocytosis of lymphocytes may be seen in all variants except lichen aureus, which shows : a bandlike (Lichenoid) infiltrate separated from the epidermis by a thin rim of uninvolved collagen (Grenz Zone).

2- Dermoscopy has been reported to be a useful tool for assisting the clinical diagnosis of pigmented purpuric dermatoses.[12]

NB: Histochemical staining with Perls stain (to demonstrate iron or hemosiderin) and Fontana-Masson stain (to exclude melanin pigment) may be helpful. Hemosiderin deposition in the dermis is more superficial in pigmented purpuric dermatitis than that seen in stasis dermatitis, which is a useful differentiating feature.

**Differential diagnosis :** 3

The clinical picture is often sufficient for diagnosis, but a biopsy specimen may be required to distinguish them from:

- Lichenoid variant from small vessel vasculitis.
- Angioma serpiginosum (but unilateral).

- MF (هيه early stages may closely mimic a pigmented purpuric dermatitis both clinically and histologically) → extensive Schamberg above Knee
- ACD (e.g. due to rubber or azo dyes such as Disperse Blue),
- Nonallergic reactions to topical medications (e.g. fluorouracil or eutectic mixture of local anesthetics [EMLA]).
- Drug eruptions (e.g. carbromal, meprobamate, acetaminophen, infliximab, pseudoephedrine),
- Suction-induced purpura (e.g. cupping or pressing the back against a bathtub)
- Hypergammaglobulinemic purpura of Waldenström.
- Dermal hemorrhage secondary to venous hypertension, which presents with petechiae superimposed on diffuse hemosiderosis (Fig. 23.5B) rather than the discrete yellow-brown background patches that characterize Schamberg's disease.

## Treatment

1- Instructions: Avoid prolonged leg dependency and treat the underlying venous stasis. by Compression hosiery (أفضل علاج)

Supportive: leg elevation, elastic stocki, Avoid leg depe

2- Medical ttt:

- Topical CS : helpful, especially if there is pruritus or marked erythema.
- Ascorbic acid (500 mg twice daily) and rutoside (50 mg twice daily) → SUCCESSEFL
- NB-UVB and PUVA (2008-2009).
- Griseofulvin (Tamaki et al; *Br J Dermatol.* Jan 1995)
- Cyclosporin.
- Colchicine.

Medical: vit c, rutoside, cs, Colchicine, Cyclosporine, Griseofulvin, PUVA, NB-UVB

Ruta c 60mg

vit c 1gm +

# Vascular tumors

classification

1. **Reactive :**
   - PG = Pyogenic granuloma
   - ALHE = Angiolymphoid hyperplasia ē eosinop

2. **Malformation :**
   - Cap Malformation (CM) → PWS, SP (Salmon patch)
   - Venous ~ (VM) → Venous leake, Blue Rubber Blob
   - Arterial ~ (AM)
   - Lymphatic ~ (LM) → Lymphangiom circum
   - Angio Keratoma
   - Mixed Malformation
     - Verrucous Heamangioma
     - AVM
     - Angiomaserpigenosum

3. **Bn Tumors :**
   - Infantile Haemangioma (IH)
   - Congenital ~
   - cherry Angioma

4. **Border line = low grade Mg :-**
   - Kaposi Sarcoma

5. **Mg Tm :**
   - Angio Sarcoma

6. **Perivascular Neoplasm & Neoplastic like Conditions :**
   - Glomus Tm
   - Glomangioma

7. **Telangiectasia.**

# ALHE = Angiolymphoid hyperplesia ē eosinophilia

**def:** Ben or low grade Mg T-cell proliferation ē 2ry vascular prolifera ch' by

## clinically

- Papule, Nodule, plaques

(2D) [ Dome shapped
[ Dermal

[ Isolated → may be grouped
[ Reddish - pink

site → Scalp s Neck, face (periauricular)

N.B → ALHE = Pseudopyogenic Granuloma

rarely ↓ - LN, Mouth, Tongue
Bone, Testis

## Histopathological

→ Endothelial cell proliferation ±
Eosinophilic infilt

→ Endothelial cell have 2 ch'

- large epithelioid or Histoid
- Vacculate Cytoplasm

NB Peripheral Eosinophilia 20%

**tt:**

- Surgical
- Laser
- IL-cs
- Indomethacin
- Isotretinoin
- Imiquimod
- Cryo
- Electro
- PDL

---

## Kimura's dse

**def** B-cell proliferative disorder ē 2ry vascular proliferation

affect: Skin, LN, Salivary gland → S.C painless skin lesion

[ periauricular - parotid - Sub Mandibular ]
ass ē LN < Single / Multiple & Salivary gland

affection at same site or distant

**path:**

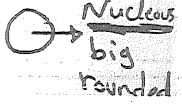
- Lymphoid Follicles & Bl-Vs proliferation ē Hobnail endothelial cells
- Marked Eosinophilia

~~DD~~ : from ALHE

inflamm → 2ry vascular proliferation

| ALHE | Kimura's |
|---|---|
| → Vs proliferation ē 2ry inflammation | ⊙ Inflammation → 2ry Vs prolif |
| [ Western الست الغربية<br>o+ > o→ | [ oriental الرجل الشرقي<br>o→ > o+ |
| - Bn , low Mg T cell proliferation | - B cell inflamation ds ē 2ry Vs prolif |
| [ Dermal<br>Rare extra cut affection | - deep S.C<br>- affect < skin, LN, salivary gland |
| — epithelioid / Histoid endothelial cells ē cytoplasmic vacuoles ± Eosinophilic infiltrate<br>- T. cell type (H P) | - Hob Nail endothelial cell proliferation<br>- Marked ++ Eosinophilic infiltrate<br>→ germinal follicles ē eosinophilic folliculitis<br>- B. cell type<br>- less Vs proliferation |
| [ peripheral Eosinophilia (20%)<br>Normal IgE | [ ++ Eosinophilia (BL)<br>↑ IgE<br>- fibrosis |

Hob Nail Cells → bulbous like Nucleous ē Nuclear projection to cytoplasm.



# Pyogenic granuloma

**def:** Reactive vs lesion chi by rapidly growing, friable, red papule or polyp of skin or Mucosa that frequently ulcerate.

**Misnomer** ↔ No infectious agent / Not granulomatous

**Tumor of pregn** = **Eruptive Hemangioma** = **lobular Cap Hemangiom**

ot = o→ ; > child young adult

**AE:**

1- Reactive : to trauma – irradiation
2- Abnormality in bl. flow : PG in preexisting pws
3- Pregnancy
4- Drugs : sys Retinoids & Indinavir & Anti EGFR Ab.

**C/P:**

- Solitary (Red papule / polyp) – grows rapidly

→ Friable → bleed ē trauma → ulcerate

site → gingiva, finger, lips, tongue, face الأكثر صدوراً ثم الأقل

↳ ē preg

تسمى granuloma gravidarum.

- Rare eruptive or disseminated (Multible satelliate lesions) توسيع الأوعية

**H/P:**

- Prominent epithelial (Collarettes) resulting from peripheral adenexial hyperplesia or downward growth of rete ridges bridged by Flattened epidermis. كوله, مع Let Margins

→ Well circumscribed, exophytic, pedunculated proliferation of small cap – arranged in lobular pattern. تذكر كوله

**DD:**

- bacillary angiomatosis
- Kaposi Sarcoma
- Glomus tm
- [illegible]

**ttt:**

[ Surgery / Laser ] [ Cryo / Electro ] [ Sclerotherapy / Topical Tim

# Vascular Malformation

- General ch: at birth, (No) sexual * or gestational predilect, slow (Expansion) proportionate ē growth & persist for life
- Any organ can be affected, but [Skin & MM] are Commonest. ✓ ± Associated ē deeper or Extra cut involvement.

## Classification

(HL) تکبار رفع

- Slow-Flow (early onset)
  - Capillary Malformation (CM)
    - SP
    - PWS
    - Telangiect.
    - Cutis marmor.
    - Nevus Anemicus.
  - Venous Malformation (VM)
    - V. lake
    - Blue Rubber Blob
    - Glomovenous malf.
  - Lymphatic Malformation (LM)
- Fast-flow (Latent)
  - Arterio-Venous Malformation (AVM)
  - Arterial Malfs. (AM)
- slow or fast Flow
  - Combined Malformation
    - KTs (CLV)
    - Prtes Weber (CLV-M)
    - Maffucci (LV)
    - proteus (C&V)

(PWS ئیز)

## Vascular Birth Marks

(سرخ رنگ)

| | Infantile Hemangioma | Vascular Malformation |
|---|---|---|
| Def. | Cellular proliferation (Tm) | Errors in vascular Morphogenesis |
| Epidemiology | More Common in: premature, F > M (3:1) | (No) Gender or Gestational predilection |
| Lesion: | Not at birth (3-5 ws after birth) → rapid prolif. → Involution. Elevated | at birth → slow expansile proportionate ē growth → persistent. Flat. (↕ become Nodular ē Age |
| Pathology | Proliferating: Endoth. Hyperplasia, lobule formation, Mast cells, Prominent BM. Involuting: Fibrofatty replacement ↓ Mast Cells | Depends on the Type: Ectatic irreg. ↕ Vascular channels. (NL Cell prolif = -ve ki 67). |
| Immunohistoch. | GluT1 +ve, Ki 67, FCεRII | all are (-ve) (ki 67 → marker ↓ cell prolif) |

Cap Malformations → plus SP Nevus Anemicus
Telangiect

1 Salmon patch :

Nevus simplex = MTN Medial Telangectatic Navus = Fading Macular Stain

- 40-50% Newborn
- irregular patches from Salmon pink to red color
- affects → glabella : Angel's kiss & Aigrette of forhead
  → occiput – Nape of Neck : Stork bite
  → Lambo Sacral : Salmon patch
  → eyelids – Nose

Fades by 1-3 ys
↳ Reassurance

but Nape of Neck lesion → persist to adult 50%

- d2 dilitation of dermal Cap

---

2 Port Wine stain :-

Nevus Flammeus = Lat telangectatic Nevus (LTN)

---

3 Navus Anemicus :

~~DD~~

xx bl. flow

VC & ↑ hypersensitivity to catecholamines

DiasCopy → fade of it's edge

(Hot – Minor Trauma) → No change

Vitilgo → Smooth

glass - slide

Nevus depigmentosus

xx Melanin Pig & Melanocytes

No change

✓ Erythema

Port - Wine Stain = Naevus flammus
= LTN

cf = low flow cap Malformation

lp = Cong — Maybe aquired
Flat — ~ raised ē ↑age (Nodular)
Segmental — ~ localized

distributed at Trigemenal N branches (3) V1 ophthalmic → forehead, lower eyelid, upper ~.
V2 MaXillary
V3 Mandibular

- Bright-red patch that blanché ē pressure.
- Face, extremeities never follow blasekha lines
→ Macrochelia → ↑ lip size (إذا علوي الدموي)
→ GNAQ Gene Mutation [encodes Gprotein α subunit]

clo - Indulation - irregularity - Thickening → ttt ē No effect
Should ttt as early as possible.

PWS assé

dis

1- Glaucoma
2- Neurological disorders [Motor, hemiplegia; seizures; MR]
3- skeletal disorders → Spina bifida
4- Cutenous ~ (phakomatosis) jeî

1- Glaucoma + CNS dse ← MRI ē gadolinium, CT, SPECT, PET
- ass ē ophthalmic branch affection
follow up by eye examination Regurally
↑ risk ein 1st (2 yrs)
(30-50%)

2- Maxillary - Mandibular branch affection → ↑ growth of Lips - Tongue - Maxilla

Syndromes

1- Sturge - Weber syn
2- Parkes - Weber syn
3- Klippel - Trenaury syn
4- Proteus synd
5- Megalo. encephalo - Cap Mali
→ PWS
→ persistant Salmon patch
→ Macro Cephaly
→ Asymm - overgro with

- **Skeletal disorder** :

- Midline PWS → lumbosacral, dorsal, Nape area

Hall Mark of Spinal dysraphism — ass ē

pit – dimple – sinus – cleft
tail like fibroma – lipoma hypertrichosis
Melanocytic Nevus – Congenital

US → 3-5 mon
MRI → most sensitive

---

- **Cut - disorders**

1- phakomatosis Pigmento-vascularis [PPV] = twin spotting

Cap Malf + Melanocytic or other Nevus

type 1 → CM + epid N
type 2 → CM + dermal Melanocytosis (±) Nevus Anemicus
type 3 → CM + Nevus Spilus (±) Nevus Anemicus
type 4 → CM + dermal Melanocytosis + Nevus Spilus (±) NA
type 5 → ē Cutis Marmorata telangectesia Congenita (CMTC)
+ dermal Melanocytosis + type 1

---

2- phakomatosis Pigmento-Keratosis :-

Nevus Sebbaceous + epid Nevus + Spilus Nevus

---

3- Angio lipomas = asympt - non infiltrating

- May be underlying Cap Malformation ↔ trunk, Pelvic girdle
- Laser - Resistant Cap Malf (CM)
- Fake

NB — phakomatosis → inherated dse affect → skin, eye, CNS

---

PWS → CNS : MRI - CT.
eye : examine Regularly.
Spina bifida : MRI.
Phakomatosis : examine skin.

# PWS assé Synds

## 1] Sturge - Weber synd :

(3) Cap Malf
- Skin → PWS
- Eye → glaucoma , Conj congestion , choroidal angioma
- CNS → Neurologic disorders

CT (Ch)

(2) both ophthalmic & Maxillary affection.
both eye lids ∿.

- seizures ∿
- MR
- Hemiplegia

(1) X-ray → double Contoured Calcification (Tram-Track)

## 2] Klipped Trenaury synd :

(3)
- CM → PWS of LL
- VM → Cong V.V
- LM → fluid filled cysts

- hypertrophy Bone , soft tissue
- Limb asymetry < gigantism / shrinkage = scoliosis
- Cellulitis
- Thrombosis
- Embolism
- Cut - ulceration

(Clo)

## 3] Park - Weber synd :

as klipped + A-V Malformation → Thrill → asse (HF)

## 4] proteus synd : = Elephant man dse

(3)
- over growth bone , soft tissue
- Birth Marks [PWS ∿ - CT Nevus - cribiform hyperplasia epid Nevus ∿]
- others
  - lipoma
  - CT Nevus → ch
  - ch facies → enlarged occiput, ptosis, Long narrow face, open mouth at rest, upturned Nostrils
  - CALM
  - choristomas of eye

## 5] hyperkeratotic CVM :

[TS - [Sturge - Weber syn - [Nevus Seb - Ant. - telangiectasia

# Lymphatic Malformation

## * Lymphangioma Circumscriptum (LAC)

**def:** Cong lymphatic Malformation localized to area of ← skin, s.c tissue
d/t structural abnormality

**C/P:** Fluid filled cysts or vesicles
discrete (or) grouped
smooth (or) warty
translucent → Red → blue black
(Bloody filled)

Frogspawn

اماكن ← Axilla, Neck, Groin

(±) Lymphorrhea

---

**Tt:** Radical excision الأفضل

- IL cs
  - Propranolol
- Laser
  - Cryo
  - Electro
- (IL)
  - hypertonic Saline
  - Pici basil
  - Doxycycline
  - → Silendinafil

---

**Invest:** (1) MRI: to avoid Recurrance after excision

(2) Immunohistochemical :-

| Lymphangioma | Hemangioma |
|---|---|
| Weak (+ve) VIII factor | (+ve) factor VIII endothe |
| discontinous Basal lamina | Multilayer Basal lamina, NL Bl.vs |
| Anti CD34 (-ve) | Anti CD34 (+ve) |

هشيل قد ايه
عشان تحدفين

---

**Co:**

1- Cellulitis like Reaction
2- Cervicofacial Bony distortion
3- oropharyngeal obst
4- Gorham-Stout = disappearance Bone dis
= visceral lymph angiomatosis + osteolysis.

---

**NB**

**deep Cavernous Lymphangioma**

- deep form of LAC.
- → extensive illdefined swelling.

deep

**Cystic hygroma**

- → Large cystic space
- → Axilla & Neck

# Sup Lymphatic dilitation

## Cong Malformation

**LAC**

- Birth

## aquired

2ry to ← Radiation / Mastectomy

**Lymphangectesia** = Aquired Lymphangioma

Adult ← **Aquired lymphangioma = lymphangectesia** → ē lymphoedema

= — lymphatic interruption: - Cellulit - Crohn's metasta

**E:** → Traumatic injury to previously Normal lymphatics :—

1- Radical Mastectomy.
2- Radiation from Mg.
3- Metastatic LN obst.
4- Scarring Processes ← Infilt. / Keloid. / scleroderma. / scrofuloderma.
5- Rare Causes

♂ - Penile ← Transient after circumcission / Elderly → ēaut evidance of obst

♀ - ē Pregn
- Cirrhotic Ascities
- AbNL dermal structure & function ← Photoaging. / steroids.

---

**C/P:**

as LAC on back ground of lymphoedema.

**H/P**

Large dilated lymph _vs ē Flat endoth - Cells

Papillary / Reticular / deep (rare)

dermis

+

epid changes ← Acanthosis / Hyperkeratosis

Abscent S.C muscle coated Cisternae.

LAC ~~DD~~ by H/P

**Tt**

1 — Compression
2 — locally destructive Methods
3 — guard against inf

**Venous lake :-**

- bluish papule on (lip - oral cavity) & soft, Compressable fill ē dependency

→ use sun screen

**DD**

- Mg Melanoma
- Kaposi Sarcoma

by dermoscopy

**Clo**

- Thromboembolism.
- IV Coagulopathy

lips → libial incompetence
check, Tongue → Abnormal Jaw growth
pharyngeal → obst, sleep apnea
limb → under / over-growth
Joint affection
bone clo

**DD**

- deep IH
- KTS

**Invest**

Doppler US - MRI → extent of lesion, Nature
Blood tests → Coagulation

**ttt**

1 - Compression garment
2 - Aspirin
3 - Laser
4 - LMWH
5 - surgical
6 - sclerotherapy

Followed by

**Synd asse VM**

**Blue rubber bleb Naevus Synd (Bean Synd) = BRBNS**

الجلد

widly disturbuted Small dark blue papules and skin Coloured Compressable Protuberances (rubber bleb)

الترسب واحدة

**Large VM**

- **GIT** lesion → bleeds → Iron ↓ Anemia
- CNS
- Lung
- heart

less Common

**Maffucci Synd**

① VM (blue to skin Coloured)

② Enchondromas

hamartomatous proliferation of chondrocytes → Abn ossification of diaphysis & Metaphysis

③ Cosmetic & orthopedic clo

site

- Extremities
- Cephalic lesion ← eye clo, CNS clo

# Angio Keratoma



**def** : group of disorders ch' by

**Clinically**

asymptomatic hyperkeratotic Vascular lesions

**Pathologically**

1 - Hyperkeratosis
2 - Sup papillary dermis Vascular ectasia
except circumscriptum Capi lymphatic Malfor
3 - dilated bl.vs

**clp**

- Soft
- Compressible
- pink-red

} Papules

3-5 mm
ē hyperkeratotic epid

**Types** :- [احفظ النوع / المكان / assē]

**1 Angiokeratoma of Mibeili** → extremities ± AD

Bilat Symetrical → dorsum of Hand, Elbow, Knee

10 - 15 ys
o+ > o→

→ assē → Chillblains.
Acrocyanosis.

**2 Angio Keratoma of Fordyce** → genital

* Scrotum - Vulvae elderly > 50-60 ys

assē Venous obst

o→
- Varicocele ✓
- Hernia ✓
- Prostatitis

Thrombophelibitis

- Sever bleeding ⓔ Minor trauma.

**tt** : Electro / Cryo

[3] Angio Keratoma Circumscriptum : AKc L.L الوحيدة جدا الاكتساح طول (13)

at birth – infancy – childhood (F) > m

clp
papule
- linnear
- hyper-Keratotic (±) Bl, lymph filled cystic Nodules
- Verrucus

site < L.L - foot
thigh - buttocks

assē
1 → Navus flammus (pws)
2 → Klippel T Syndr
3 → Haemangioma
4 → Angiokeratoma of Fordyce

D → H/R → lymphatic Component
أقوى
- Early age

---

Soliatry Angio Keratoma :- L.L

at extremeties (L.L)

assē → trauma, Injury, irritation

DD → Wart
M.M

---

Angio Keratoma Corporis diffusum : = Fabry's dse

a.f: XLR disorder ch' by deficiency of lysosomal enzy
∝ glactosidase A
↓
accomulation of glyco sphingo Lipids (ceramide Trihexoside)
in fluid, Visceral organs
↓ endothelia, peri thelial sm
Metabolic dse

clp
الأكثر

Eye
- Corneal opacity.
- dilated Conjunctival Bl.Vs & Tor us
- upper eyelid oedema. Constricti

Systemic
- Fever
- RF
- HTN
- CNS – CVS Stroke
→ acroparathesia.
(Sever pp burning pain)
parasthesia ē episodes (F)

Skin
Angio keratoma
↑ No – disseminated (Rosett Grou
generalized, Small size
less hyperkeratotic bathing Trunk
() knee & umbilicus
Xerosis — Anhidrosis

DD → fucosidosis

I-:
1- skin biobsy → ↙ dilated bl.Vs in upper dermis éch' ch' ↙ Vacculated endoth cell → lipid
2- Urine → (RF) albuminuria – Heamaturia – proteinuria – lipophages
3- ↓ ∝ Galactosidase A → PAS (+ve) Maibeky like × Cells → urinary section
in plasma – WBCs – Fibroblast

T-:
1- Laser (Angio Ker...)
2- Aspirin (Stroke)
3- Tegretol (Pain)
4- Human Recombinant ∝ galactosidase A
5- Gene therapy

# Treatment

(Ref: 2 · Bolognia · JH · IJDVL)

Active = non-intervent

1. Reassurance: about Nature Course & Spont. Involut

2. Medical JH · (A) Topical
   - IL Cs
   - Topical Cs
   - Imiquimod
   - Topical BB
   - (DNNZ) Becaplermin gel.
   - Eosin (antiseptic & antiangiogenic)

   (B) Systemic
   - BetaBlocker
   - Corticosteroids
   - IFN α
   - Bleomycin
   - Angiogenesis Inhibitors (Future JH)

3. Surgical JH:
   - Compression
   - Sclerosing therapy
   - Embolizat°
   - Laser
     - Cryo
     - Radio
     - Excision.

(4.) JH in specific situat°

---

- Discussion of JH

  - Cs: the 1st line of JH. (Now BB)
  - Mechanism: ?? but ± d.f.
    - i - VC
    - ii - Antiangiogenic
    - iii - (++) Apoptosis
    - iv - regulate Cytokine expression.

Types

- Topical (superpotent Cs)
  - For uncomplicated localized lesions.
- Systemic
  - For large, deforming, Life threatening & persist. with ulcerated lesions.

Functional

## Topical Cs

- Topical Cs (Controversy) → Superpotent
  - Used: For periocular lesions??
- IL Cs → Effective
  - 5-40 mg/ml Triamcinolone
  - dont Exceed 3-5 mg/kg/session. (4-6w)
  - C.I: periorbital

## Systemic Cs

- Indications: as before (given during proliferative phase).
- Prednisolone → Dose: 2-3 mg/kg/d for either 2-3 ms or until growth stops or shrinkage occurs then → Gradual withdrawal [Mean period 8 ms]
- S.E:
  - GR
  - Axis suppression
  - personality changes (irritability & sleep disrupt).
  - Immunosuppression
  - life threatening inf. ]
- others:
  - GIT symptoms
  - Cushingoid
  - Neurotoxicity (d/t the preservative Benzyl Alcohol)
  - ↙ Live-virus vaccines

BB Better Than Cs because Rapid Relapse after Cs stop. while BB effect is maintained.

≥ 2mg/kg For > 2ws.

- For large; life or function threatening lesions that resistant to systemic Cs → IFN $\alpha_{2a}$ or IFN $\alpha_{2b}$ 3 million U/m2 (daily) For 6-12 ms. if Failed →
  - Cyclophosphamide
  - Vincristin
  - Bleomycin
  - Propranolol
  - Embolization

# Infantile Haemangioma

**Epid :**

[ 70% 1st few weeks of life (3-5 ws)
30% at birth (Cong)

♀ > ♂ → 3 : 1

↑ ē ← Premature, LBW, Fetal Hypoxia

- Caucasian
- soft tissue , vascular Tm of infancy.

---

**Clp = phases**

**1 Nascent phase** = Precurser lesion — at birth

[ Erythematous Macule
Telangectatic Macule ē pale Halo

rare [ Bruise & Scratch
ulceration → lip – perinium

---

**2 proliferating phase** (Max 4-6 mon) خلال أول سنة

lesion → Macule , Papule , plaque [0.5 – 5 cm] size

site → H&N > Trunk > extremities

color

1 **Sup** (sup dermis , pap dermis) — 2 **deep** (deep dermis – S.C)

Bright red (أحمر) / Crimson

Strawberry lesion 50-60%

blue / purple (أزرق / موف)

Cavernous H → warm mass 10%

3 **Mixed** → blue ē Telangectasia 30%

Pattern
- Localized
- Segmental
- Multiple = disseminatted

فوق / تحت

No.
- usually Single ± Multiple
  - ↓ Neonatal H

**Stationary phase** :- (12 - 15 mon)

No change in size

**Involuting phase** :- (>15 mon)

Slow ↓↓ Size
pale grey & ↓ Firmness.

**Involuted phase** :-

Untreated lesion → 90% → 9y, 70% → 7y, 50% → 5y, 30% → 3y

& → (50%) Normal skin → Sup type
(50%) Abnl skin → - Telangect, - stipple scarr, - Anetoderma, - Redundant skin, - Fibrofatty resid, - Hypo pigm

**No of lesions**

- < 5-10 → Multiple IH
- > 5-10 → Miliary / Neonatal H
  - (+) Visceral H → diffuse Neonatal H → CNS, GIT, Liver; (MR) 30-80%; ↑ Cop HF; Jeje d2 [ Hypothyroidism
  - (X) No Visceral H → Bn Neonatal H

**VB** :-

A- Minimal / Arrested H = (No) proliferation phase or <25% of surface
(c/p) Reticulated erythema + Telangectesia
large ectatic vs + Some bright red- Papules

B- Cong Hem

**IB**

Recent pathogenesis :-
Endothelial progenitor cells (EPC)
- Circulate in fetus
- disappear at birth
- Jeeé Remain in LBW, premature

Hypoxia of baby → ++ EPC → Haemangioma

disappearance of EPC → Regression of IH

Clo

① **Ulceration** : Most common (1%) ē ḍeg̃.

assē → bleeding, infection, Scarring

3 site → Lip, Neck, Anogenital

3 types → Large, Mixed, Segmental

---

② - **Interfere ē function** :- (5) نادر

* periocular → visual field dis, Amblyopia, Astigmatism, proptosis

* lip → ulceration, feeding diff, disfigurement

* Anogenital → ulceration, Bleeding, Painful defecation, urination

* External Ear → Conductive deafness

* Nasal tip → Sup : ulcer, scar

deep, Mixed : cartilage distortion — Cyrano Nose

---

③ - **Heart failure** (HF) : ↑ Cop (dz) shift of bl to skin

ē visceral H esp ē liver H

ē diffuse H

NB Hepatic H ↔ HF. hypothyrodism.

MRI اعلى

---

Invest

1- US

2- MRI

3- GluT-1

④ - **hypothyrodism** :-

dz ↑ Indothymin deIodinase (in Haemangioma) -- thyroid hormones

assē → Large cut H, Hepatic H

⑤ assē visceral H — Thyroxin level ↓

## Syndromes ass ē IH :-

pHACES
Lyngeal
LUMBAR
PELVIC

### 1 PHACES → sternal cleft

- P → Post fossa + brain
- H → Haemangioma
- A → Angiomatosis + Arterial Anomalies
- C → Cardiac Coarctation of Aorta
- E → eye endocrine anomalies
- S → sternal cleft

---

### 2 LUMBAR

- L → lower body Haemangioma
- U → Urogenital Anomalies
- M → Mylcopathy Spina bifida
- B → Bone deformity
- A → Anorectal Anomalies + Arterial
- R → Renal Anomalies

MRI

---

### 3 Laryngeal – low face haemangioma :

[ ass ē Cardiac Anomalies
Air way obst / RD.

ENT

---

### 4 Kasabach – Merrit synd :

1 - rapidly growing Vascular Tm
- Kaposiform Haemangio endoth -ioma
- Tufted angiomas
- rarely cut Haemangioma

△ 2 - Thrombocytopenia ⇄ Petichae Purpura

3 - Consumption Coagulopathy.

MR 20%

ttt → Replacement therapy
- Cs - Vincristine - cyclosphosphamide. Sirolimus (chemotherapy.)

Called = Haemangioma – Hge syndrome

NB → May occur ē Klippel synd.

---

### 5 PELVIS

Synd :-

- P → perianal H
- E → ext genitalia Ab NL
- L → Lipo Myelo Meningocele
- V → Visceral Ab NL
- I → Imperforated Anus
- S → skin tags

# Tt of IH :-

- **Topical**
  - IL Cs
  - Topical Cs
  - Imiquimode
  - Topical BB
  - Aldara
- **Reassurance**
  - Spont Involution
- **Systemic**
  - BB
  - Cs
  - INF α
  - Bleomycin
  - → Angiogenesis inhibitors
- **Surgical**
  - Cryo
  - Radio
  - Excision
  - Compression
  - Embolisation
  - Sclerosing therapy.
- **Lasers**

---

1. **Reassurance** :-
   Nature & Involution spontenously

2. **Medical Tt** :-
   - **Topical**
     Uncomplicated Localized lesion
   - **Systemic**
     Large – deforming
     Life therating – persistin
     Ulcerated lesion

---

## Cs

Mech
- VC
- Anti angiogenic
- ++ Apoptosis
- Regulate Cyto Kine expression

CI
- Cs عند الأم وقفل
- live virus vaccine
- Perioral !?

- **Topical** → Super potent Cs
- **IL Cs** → 5-40 mg/mL (Triamcinolone) (or until growth stops) 8 mon
- **Systemic** → 2-3 mg/kg/d for (2-3 mon) (4-6 w) then (gradual Withdrawal)

SE
- Immuno suppression / GR
- life therating Infect / AXis suppression
- Personality changes, irritability, sleep disturbance
- GIT Sympt
- Cushingoid
- Neuro toXity (≥ 2mg/kg for > 2w)

given during proliferative phase

(d2) perservative Benzyl Alcoh

NB Live_Virus Vaccine → (Not) before stop Cs by 1 mon.
بعد ما أوقف بشهر على الأقل

if large , life therating , Cs Resistant lesion :-

Use INF $\alpha_{2a}$ — INF $\alpha_{2b}$

3 million U/m2 daily for 6-12 mon

if failed

- Cyclophosphamide
- Vin Cristin
- Bleomycin
- Propranolol
- Embolization

Mech → Antiangiogenetic

SE →
- Neutropenia
- Fever
- ↑ liver Enz
- flue like sympt
- irreversable Neurotoxic Spastic diplegia

---

BB

قبل ما تبدأ لازم echo

Mech → VC, VEGF ↓↓, ++ apoptosis of endothelial cells

SE →
- 2B ↓ → Brady Cardia, Bronchospasm
- 2H ↓ → hypotension, hypoglycemia
- Mask manif of HF

dose 2mg/kg 1 day

2-3 times bet day

6-12 mon

to avoid Rebound Tachycard

ē gradual Withdrawal 3 w

لازم يرفع كل ٣-٤ ساعات وتأخذ الدوا بعدها

لازم HR < 100 اثبت الجرعة

CI
- Bronchial Asthma
- Cardiac dse
- CNS Vascular Anomalies

* ++ ulceration Healing → Can use ē ulcerative type

| inpatient | outpatient |
|---|---|
| age - < 8 w | - > 8 w |
| - Comorbidities < CVS CNS glucos Reg | - No Comorbidities |
| - Non Co-operative mum | - Cooperative mum |

---

Laser

ND-YAG

deep & Mixed lesion

pulsed-DYe (PDL)

Sup - ulcerating - Residual

SE < ulceration, dyspigm, Scarring

↑↑ risk for SE

# Surgical ttt

- involuted or partially ~ lesions
  - to Remove fibrofatty tissue & Redundant skin
- proliferating
  1. Pedunculated lesions
  2. Recalcitrant pericular lesions
  3. Recalcitrant ulcerative Lesions

---

## Cherry Angioma

Cample_De Morgan spots = Senile Angiomas

**def:** Most Common aquired Vs proliferation.

**clp:**
- Bright red
- dome-shape
- polypoidal papules

site: trunk, upper extrem

**asse:**
- aging.
- pregnancy.
- POEMS Synd. → Glomerioloid Haemangioma

**Hip:** Congested ectatic Caps & post Cap Venules (papillary dermis)

---

| IH (infantile H) | RICH (rapidly involuting Cong H) | NICH (Non involuting Cong H) |
|---|---|---|
| * Absent _ per-cursor _ present (at birth) | * fully developed | * Fully developed |
| * Rapid postNatal proliferation | * Intra uterine proliferation | * Proportionate growth |
| * low spont involution | * Rapid involution >1 yrs | * (Not) involute Spont |
| ↑ (> girls) | (equal) but (>girls) | ↑ more (> boys) |
| lobular endothelial proliferation during proliferative phase<br>fibrofatty tissue ē involution | * Cap lobules within fibrotic Stroma Containg thin Walled Vs, hemosiderin. | * lobules of small, thin Wall Vs ē large Central Vs dilated, dysplastic Veins<br>() lobules<br>(Rabnait) endothelial cell. |
| Glut-1<br>Lewis-y Ag (+Ve) | (-Ve) | (-Ve) |

# Kaposi Sarcoma

Is it Neoplasia ? (21)
or hyperplasia ?

Low grade Mg Tm

**def :** Rare, Multifocal low grade Mg / Bn Tumor of vascular endothelia tissue Can affect ← Skin, m.m, L.N, Viscera ← GIT, Lung, Liver

Not Metastasis
Multifocal orgin
[chem > surgery]

**E :**

1 onchogenic viruses :-
- CMV
- HPV 16
- HHV 8 (Ks ass Herpes virus)
- HIV

**types :-**

1- Classical Ks = Speradic
2- Endemic = African type
3- Epidemic = (HIV) ass Ks
4- Iatrogenic = immunosuppressive ass Ks
5- Familial

**athogenesis :**

This viruses Infect [CD4] → Release of Angiogenetic growth factors & Cytokines → TNF, IL 1 & 6

HIV1 transcripting Gene (Tat)

Ks ass HIV

(40%) → AIDs
(95%) → homosexual
(5%) → others Methods of infections

♂ : ♀ in HIV Ks
100 : 1

**Clem**

| | | | ♂ : ♀ |
|---|---|---|---|
| 1- Classical | eastren, Western Jewish Mediterrian background | 50-80 y | 15 : 1 |
| 2- Endemic ← Bn nodular aggressive florid lymphadenopathy | Black afferican ← adult / child | 20-40 ys / 2-15 ys | 15 : 1 / 3 : 1 |
| 3- Iatrogenic → immunosuppressive | SLE transplant (Renal Recepiant) lymphoma | 20-60 ys >3-30 mon after transplant | 3 : 1 |
| 4- Epidemic (AIDS) | ← Homosexual Men 95% / other risk group 5% | 20-60 ys | 100 : 1 |

## 1 Classical Ks :-

(3) age → 50 - 80 y
Sex → ♂ : ♀ (15 : 1)
race → Europian – Eastern – Jewish

(3) Skin, LN, Visceral → (10%)

(3) Behavior: Course, survive, death

* Bluish-red or dark Brown-Nodules & plaques May be :-
  - Hyper-Keratotic / Verrucus
  - Annular / serpigenous
* Affecting distal extremeties
* Actal Nodules, plaques

Visceral: GIT, Liver, Lung, Abd LN, Heart — 10%

Course :
(3) Indolent; slowly progressive; Spont Resolution → pigmented Scars

Death : (10%) after 10 ys.
GIT Bleeding, Ulceration, Visceral involution

10% → Visceral, LN, death 10 ys

---

## 2 Endemic Ks :-

age → 20 - 40 ys
Sex → M:F (15 : 1)
race → African (black)

in children (2-15 y) (3 : 1)

C/P (4)

- Nodular
  - 25-40 ys
  - (15) classical Ks
- Aggressive = locally
  - large Exophytic Nodules Fungating Tm of lower extremities (locally)
  - (−) LN → rare
  - (±) visceral → Sometimes
  - Behavior → prog ↑ in lesion & destruction of tissues & bone.
  - Survive → 5 - 8 ys
- Florid = dissimenated
  - dissimenated Nodules
  - (±) LN / visceral → Sometimes / Early
  - Behavior → Rapid progressive, locally aggressive
  - → Early visceral
  - → 3-5 ys
- Lymphadenopath = LN
  - Children
  - ↓ Minimal skin affection
  - ↑↑ Marked LN & visceral
  - Rapid progressi
  - Fatal ein -
  - → 2-3 ys

## 3 Iatrogenic KS :-

- age → 20-60y
- sex → M:F = 3:1
- race

- Skin → disseminated patches, Nodules, plaques
- LN → rare (-)
- visceral → Frequent

Behavior ↙ Indolent
↘ Regressive (ē) stop drug.

AE: Immunosuppression, Transplantation

---

## 4 Epidemic KS :-

(STDs induced by Viral factor) co- اثبات

- Age → 20-60 ys
- Sex → M:F = 105:1
- race → HIV ptn

- 40% of HIV → KS
- 95% → homosexual
- 5% → hetero sexual, other
- Common ē → advanced Immunosuppression → CD4 < 400

- Skin → differ from Classical in:-
  - أصغر Smaller
  - أسرع Rapid progression
  - على الجانبين Bilat - Symmetrical - Extensive
  - على الخط Along line of skin cleavage ← Trunk, Face
  - أقل slight infilt ← patches, plaques, Nodules

Nose Tip ← predilection site

- MM → oral (جديد) Maybe (1st) affected site ↳ Hard palate
- LN → Frequent
- visceral → Frequent > maybe (ē) absent skin aff.

Behavior →
- Rapid progressive
- Survive 3m-5ys
- death (Not) from Ks but Infection (أقوى)

## Staging Classification for AIDS Related KS :-

| | Good Risk (0) | Poor Risk (1) |
|---|---|---|
| Tumor (T) | Skin & or LN & or Minimal oral affection ↳ (Non nodular / palate) confined to | ↳ oedema / ulceration ↳ Extensive oral affection. ↳ GIT. ↳ Non Nodal visceral affection |
| Immune-system (I) | CD4 ≥ 200/μL | CD4 < 200/μL |
| Systemic illness (S) | (-Ve) opportunistic infect & Thrush (-Ve) B Symptoms performance status ≥ 70 Karnofsky | (+Ve) (+Ve) < 70 + other HIV Related illness ↳ Neurologic |

B Symptoms → [ Unexplained Fever, night sweats
[ > 10% involuntary wt loss
diarrhea > 2 wks (persistant)

---

**Pathology :-**

**Early lesion** (Macules)

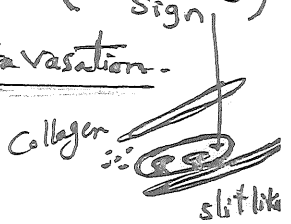
- (G.T) Granulation tissue like
- Large No of dilated caps & endothelial cell proliferation (protrude in the lumen)

**Late lesion** (Nodules)

① - Neoplastic spindle cell proli (Spinus Vascular Spaces)

② - slit like Vascular spaces
() Collagen & protrusion of the newly formed Bl Vs in lumen (promontary sign)

③ RBCs extravasation.

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**Invest :-**

① HIV ← Serology, viral load, CD4 count

② CXR = chest X-Ray (Mets visceral)

③ occult Blood in stool

④ - LFTs
- RFTs
- CBC

## Immunohistochemical stains :-

① Non specific endothelial marker * CD 34 + , $CD_3$ +ve

② Lymphatic endothelial Marker * D2-40 (podoplanin)

③ specific stain * Anti HHV8 Nuclear Ag

**pulm invest :-**

1- CXR
2- Bronchoscopy
3- CT Thallium & Gallium

Q to diff ① pulm KS infection ← intense Thallium Gallium (+) No (-)

---

## TT of KS :- Aim ← Cosmosis palliative -- progression

### Limitted ks

① lesion < 10
② No ← visceral / oral
③ Absent (-ve) Tm ass Lymphoedema

### Sever = Disseminated KS

① No > 10
② (+) ← visceral oral lesions
③ (+ve) lymphoedema
④ Resistant limitted Ks (~II)

- Cryotherapy
- Radiotherapy
- Alitretinoin gel
- IL - vinblastin.

**Chemotherapy**

**IV Infussion**

- Liposomal anthracyclines :-
  - PEGylated liposomal doxorubicin
  - liposomal daunorubicin
- Texanes (paclitaxel) IV infusion
- IFN-α

---

**HIV Related :→**

① HAART (±) لورده تحفي
② IFN α (±)
③ Radiation

Texanes Anthracyclines
if worsen after HAART (Immune Reconst Synd)

**DD :- pseudo Kaposi** ← stasis ecz

**oral lesions :-**

- IL Vinblastin.
- Sclerosing agent.
- Systemic therapy.

**other lines of ~~tt~~ :-**

- Thalidomide
- Foscarnet
- Sirolimus
- Imiquimode
- Matrix Metallo proteinase inhibitors col-3
- PDT
- Surgical

**def:** highly Mg Tm of vascular endothelial cells

**5 types**

- face & scalp
- rare death:
  - ass ē chronic lymphoedema following radical Mastectomy
  - epithilioid Angio Sarcoma (Stewart-Treves synd)
  - post irradiation بعد الاشعاع - اسوء نوع

**C/P**

- elderly — H&N (face - scalp)
- erythermatous (or) Hge bruise like Macules and plaques

Cellulitis like

**Prognosis**

[die ein 2-3 ys d/t Metastasis
bad Prognosis → (12% survive for 5ys)]

**Tt**

- surgical excision !? [Multicentric, extensive, rapidly growing
rarly successful]

---

## glomus Tumor

**def:** Bn Tumor arising from glomus body in AV shunt called Sucquet-Horer Canal. → [Modified Smooth ms cells]

Function :-

1- shut bl away from skin when exposed to cold to prevent heat loss

2- Allow Max bloodflow to skin in Hot weather to ↑ heat loss

present in dermis surr by Capsule

digit of finger-toes (esp) subungal تحت الظفر

---

**C/P** types: ① Solitary ② Multiple ③ visceral

at 30-50ys

1- small / pink / painfull / Nodule

2- pain
- Spontenous 80%
- Touch 100%
- Cold exposure

3- Most Common sites : Fingers - Toes - penis - H & N

4- ± Nail deformity

**Multiple Glomus Tm** (Glomangioma)

Large , dark blue , deeper in dermis , Not Painfull

± AD (Mutation in globulin Gene in ch-1)

Subtypes : 1- Localized → grouped at one area as extremetis
2- disseminated → No grouping.
3- Cong plaque like

---

**H/p** :

**Solitary**

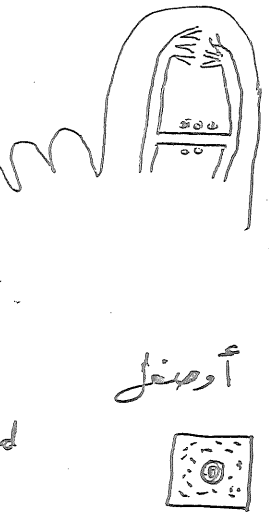
- Nodules Well defined
- Solid
- Endothelial lined VS spaces surrounded by clusters of
- glomus bodies & rim of Fibrous Tissue.

(Cellular) ↑ glomus cell

**Glomangioma**

- ill defined, less Solid Nodules!
- large endoth lined VS channels Contain (RBCs)
- Glomus Cell (Smaller) present in Walls & arround channels in clusters.

(Angiomatous) ↑ VS space



أو ممكن



**Clinical Tests** :

① Love test : Pin or pincile tip (pressure or touch)
100% Sensitive , specific exquiste local pain

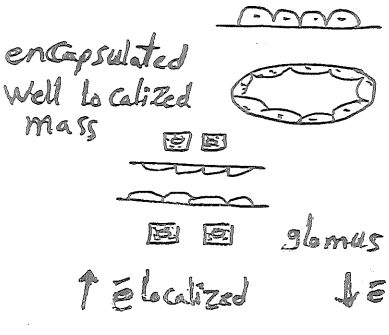
② Hibiketh test : ↓ pain induced by love test
by inducing Ischemia by tourniquet
(-ve) No pain on touch ← برفع ايده و بربط تورنيكيه
Sever pain بالتالي

③ Cold Immersion :

---

**Glomus Cells**

- Cuboidal
- N - Central - plump Nucleus
- C - Eosinophilic Cytoplasm.



# TELANGIECTASIAS

Abnormal, small, persistently dilated blood vessels visible in the skin (Fig. 106.7). Individual vessels can be discerned and range in color from light red to deep purple and will usually empty with pressure. They occur as a result of vascular dilation rather than new vessel growth and are thought to arise from capillaries, venules or small arteriovenous malformations.

## CAUSES OF TELANGIECTASIAS

**Primary**

- Generalized essential telangiectasia
- Unilateral nevoid telangiectasia
- Angioma serpiginosum
- Spider telangiectasias (also associated with estrogen excess)
- Hereditary benign telangiectasia[*1]
- Costal fringe

**Secondary to physical changes or damage :** Photodamage, Post radiation therapy, Traumatic, Venous hypertension

**Skin disease :** rosacea, PAV, involuted infantile hemangiomas

**Hormonal/Metabolic :** Estrogen-related (LCF, pregnancy, Exogenous estrogens) and Corticosteroids

**Systemic conditions**

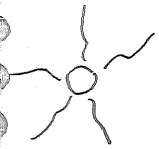
- Carcinoid syndrome
- Mastocytosis (telangiectasia macularis eruptiva perstans)
- Autoimmune connective tissue diseases : SLE, DM, CREST
- MF
- CBCL
- Angiolupoid sarcoidosis
- Graft-versus-host disease (in the context of poikiloderma)
- HIV infection

**Congenital malformations and genodermatoses**

- Cutis marmorata telangiectatica congenita
- Klippel–Trenaunay syndrome
- Hereditary hemorrhagic telangiectasia
- Ataxia–telangiectasia
- Hypotrichosis–lymphedema–telangiectasia syndrome
- Rombo syndrome
- Bloom syndrome
- Rothmund–Thomson syndrome
- Poikiloderma with neutropenia
- Dyskeratosis congenita
- XP

# Telangiectasias: Disscusion

- **Spider Telangiectasia:** (Nevus Araneus, Spider Angioma)



  - Central feeding arterial Vs (red central papule) ē radiating multiple small (dilated) Vs at face, Trunk & extrem.
  - occurs in: ① Healthy children & ♀
    ② Excess Estrogen Conditions ← pregnancy, OCPs, LCF.

**Tt:** Electro or Vascular laser

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- **Generalized Essential Telang.:** Idiopathic, progressive usually affects limbs of ♀ (Adult) (Trunk ±).

- **unilat Nevoid:**
  - ± Cong. or Acquired (d/t excess Estrogen).
  - has dermatomal distribut~ (d/t Trigeminal or Cervical N.)

- **Angioma Serpiginosum:** (DNMZ, Bl.gy)
  - ♀, in 1st 2 decades.
  - Non-palpable, deep red to purpule (puncta) occurs in small clusters & sheets ō may take Serpigenous outline, Annular/Gyrate or linear.
  - usually unilat at Extremities (Buttocks & Legs) Esp ē → Generalized (but spare: PP & MM.)
  - DD: Majocchi purpura (but Bilat & Biopsy)

- **DD of Generalized Essential:** Cut. Collagenous Vasculopathy: Central distrib. ē perivascular Type IV Coll. deposit~

## Hereditary Hemorrhagic Telangiect. (HHT)
## (Osler_Weber Rendu dis)

- AD condition d.t Mutat^n in 2 Genes (HL)

HHT-1 → Endoglin protein
HHT-2 → ALK-1 protein

- Both ↓ proteins are TGF-β receptors expressed on Endoth. & play role in Angiogenesis & Vs Wall integrity.

Essential. لازم

Criteria of Dx
1- Recurrent Spont. Epistaxis
2- Mucocut Telangiect. or AVMs
3- Visceral " "
4- +ve FH of 1st degree
- Definite Ø ≥ 3 - possible: 1 or 2 (esp. early life)

- Clp → Multiple Telangiectasia & AVM at:

1- Skin ← face, Hands, finger tips (نتظاهر بالبلوغ)

2- Mucosal: Lips & Nose → Child ē repeated Episodes of Epistaxis (نزيف من الأنف)

3- GIT → Hge & Anemia.

4- other organs: Lung, Liver, CNS, spleen & UT.

Skin ← Papular, Mat like

Hge ← early: Nose; late: other organs.

---

## Ataxia-Telangiectasia (Louis-Bar Synd)

- AR ; ch^ by:
  - Ataxia
  - Telangiectasia → Skin: Malar prominence, Eyelid, ears, popliteal & Antecubital fossae
    Eye → linear bulbar Conjunctival Telangiect. (أول علامة تظهر عند الأطفال ٣-٦ سنوات)
  - Immunodeficiency
  - Lymphomas..
  - GR
  - chromosomal instability (translocat^n bet 7 & 14 chromosomes)

3

# Classification of Panniculitis (4)

## Mostly Septal

- EN
- EN migrans
- Eosinophilic Panniculitis (Non-specific entity; ± ass. c EN, Scleroderma, Morphea, Atrophy, Lupus Panniculitis, Inf.)

## Metabolic Panniculitis:

- Pancreatic
- $\alpha_1$ Antitrypsin
- SCFN
- SN

## Mostly Lobular

- Lupus Panniculitis
- Enzymatic (Pancreatic) Fat Necrosis
- $\alpha_1$ Antitrypsin deficiency
- Sclerema Neonatorum
- S.C. Fat Necrosis of New-born
- Cytophagic Histiocytic
- Weber-Christian (Idiopathic Nodular Panniculitis; ♀, 20-40 → at L.L legs → atrophic depression).
- Post-Steroid
- Traumatic
- Calciphylaxis
- Gout

## With Vasculitis

DNNZ

- Small vs vasculitis
- SVV
- C-PAN (2 vascul.)
- E. Induratum (2 leprosy)
- ENL
- Lucio's phenom.
- Superficial thrombophlebitis
- Rhad & Crohn's, Behcet

## Mixed

- Sclerosing Panniculitis (Lipodermato-Sclerosis) (Cf LWF)
- Infective
- factitious
- GA (SC), NBLD, NBXG, Scleredema
- fasciitis – Panniculitis Synd.

# Erythema Nodosum

. Def. Septal panniculitis (small vasculitis), representing Hypersensitivity react- against strept. inf., TB, Sarcoidosis, IBD or it ± Idiopathic

. Etiopathogenesis: Hypersensitivity react- to stimuli:

. ﻋﻨﺪﻩ
1. Idiopathic (30-50%)
2. Strept Inf. (URT) (ﺍﻟﺘﻬﺎﺏ ﺍﻟﺤﻠﻖ ﻭﺍﻟﻠﻮﺯ) & TB
3. Sarcoidosis (ﺍﻟﺴﺎﺭﻛﻮﻳﺪﻭﺳﻴﺲ) [EN the most common Cut. Manifs of Sarcoidosis
?? Lofgren syd: (fever, Hilar L.N, arthritis, Uveitis, HLA DRB1*03)
4. IBD & Crohn's (GIT ﺍﻟﻤﻌﻮﻱ)
5. Drugs (OCPs, Sulfa, halides)
6. Others

. TB: ﻣﻤﻜﻦ ﺍﻟﻤﺮﻳﺾ ﻳﻜﻮﻥ ﻋﻨﺪﻩ TB ﻭﻣﺎ ﻳﻌﺮﻑ ﺇﻧﻪ ﻋﻨﺪﻩ developing countries ﺑﺎﻟﺪﻭﻝ ﺍﻟﻠﻲ ﻟﺴﻪ ﺑﺘﺘﻄﻮﺭ

. Yersinia, Salmonella .. deep fungal inf.

. Behcet

. Mg (Lymphoma & leukemia ﻣﻤﻜﻦ ﻳﻜﻮﻥ ﻋﻨﺪﻩ ﺳﺮﻃﺎﻥ ﻭﻟﻜﻦ ﻣﺶ ﻣﻌﻨﺎﻩ ﺇﻧﻪ ﻫﻴﻜﻮﻥ ﻋﻨﺪﻩ ﺳﺮﻃﺎﻥ)
. pregnancy.

. other: Viral Inf.

. Arthritis
. Constitutional Manifs → . CLP (any age but usually 18-34 ; M:F 1:4)
. EN

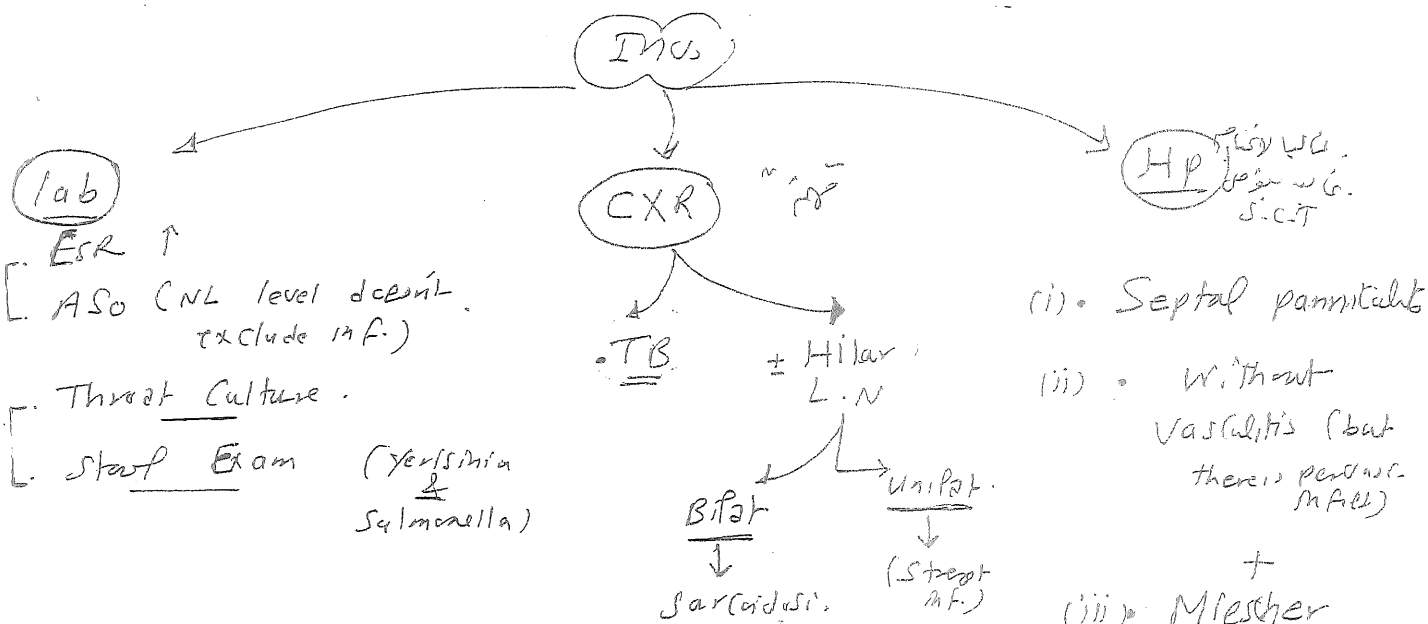
. flue like Symptoms FAHM. lasts 1-2 ds → Erupt- (2-4 ws before erupt-)

. Arthralgia ﺑﺘﺒﺪﺃ ﺑﻌﺪ ﻣﺎ ﺑﻴﺠﻲ ﺍﻟﻄﻔﺢ
Non destructive, Arcellular. usually → Ankle, Knee, Wrist.
MaX: persist for ~ 6ms.

. Erupt-: Ill defined, Indurated, Erythematous (Nodules & Plaques at any site but prefibial area is the most common) Tender
1w - 6ms → resolut- ﻣﻦ ﻏﻴﺮ ﻣﺎ ﻳﺴﻴﺒﻮﺍ ﺃﺛﺮ
in inf. Idiopath. Changes (Bluish).

. usually 3-6 ws
. but ± ↓ 1w to ↑ 6m..

NO Ulcerat-

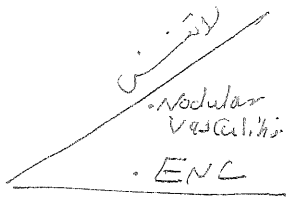



(HH)

① Underlying Etiology:
- Infect
- # drugs

② 1st line
- Bed rest
- NSAIDs
- KI (↓ ← fever, arthralgia, Tenderness)

③ 2nd line (Severe cases)
- Cs
- Colchicine
- Dapsone
- Antimalarials.



# DD of EN
## (Painful Nodules at leg)

[Annals, 7 2012]

1. E. Nodosum (EN)
2. EN. Migrans = Sub-acute Nodular Migratory Panniculitis
3. Erythema Induratum
4. Stocking → Lipodermato Sclerosis = (Sclerosing Panniculitis)
5. Linear — Superficial Thrombophlebitis
6. Linear — C-PAN
7. Others — Mg (Lymphoma associated)
   EN like lesions of Behcet.

| DD | Details |
|---|---|
| • EN-Migrans. (Chronic EN = Sub-acute Nodular-Migratory panniculitis) (Villanova dis) ♀ 30-60 (E. med.) | • Single Nodule / plaque:<br>• Unilat.<br>• painless.<br>• Enalages: peripheral extension ē Centrap Healing ē yellow hue or Morphea-form Centre.<br>• Migrate: after wks - mo. |

..H: ILC . KI (or) Systemic Cs

DD.

## Sclerosing panni-Culitis

Clipodermatosclerosis

- Etiopath
  1. Venous stasis
  2. " insufficiency & HTN
  3. Coagulopathy
- Clp (uni or Bilat.)
  - Acute stage: Indurated, Erythematous, Tender, Hot, Plaques at inner leg above the ankle. (Cellulitis like)
  - Chr. stage (Chronic): [Sclerosis]
    - Pain, Induration, redness, Hyperpigm. + VV ± leg ulcers.

(Stocking distrib = Inverted Champagne Bottle = Bowling pin.

- HP → Mixed panniculitis

- US & MRI → to define Extent of dis. & possibility of Vascular surgery.

---

- (tt) نلبس Compression Therapy لـ Venous Stasis
  1. Vein surgery (laser ablate or sclerotherapy)
  2. ↓ w.l.
  3. US tt → ↓ fibrosis.
  4. fibrinolytic: Streptokinase.
  5. Trental: ↑ Flow & Blood.
  6. Topical Cs: ↓ inflamm (early)
  7. Horse Chest-nut extract: ↓ in venous dis

## Superficial Thrombophlebitis

(Behcet) عند المرضى

- Et → Cs
  1. Prednisone
  2. Azathioprine
  3. Cyclophosphamide
  4. Methotrexate
  5. Cyclosporine
  6. Infliximab
  7. Adalimumab
  8. Etanercept

- [1] Coagulopathy.
- [2] Venous insufficiency, DVT & VV
- [3] Traumatic: IV lines infection

# Superficial thrombophlebitis

- C/P • Linear (along path of vein) ; Multiple, Tender Nodules usually at Lower legs (great Saphenous Vein).

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Tx : [ • leg elevation, Compression Stocking.
• NSAIDs, Antibiotics.
• LMWH
[ • Puncture & Evacuate → of effected Vein
• surgical - Excision of affected Vein.

Complications: Deep Vascular Dvt to IVC.

---

# Polyarteritis Nodosa (PAN)
## (Periarteritis Nodosa)

- Def. Segmental, Necrotizing, Medium Sized Vasculitis affecting Medium Sized aa commonly at their branching points (Coronary, Hepatic, renal, Cut.) → aneurysm or Stenosis

- Types — Systemic : d.t HBV
Cut. : d.t Strept. or Drugs.
[ others : • FMF, SLE, IBD • Drugs.

- C/P — Systemic (90%) : Systemic affect of aa of ← renal Carcinoma Hepatobiliary Cut.
Cut. (10%) : → Chr. relapsing Course.
• Painful S.C. Nodules along Course of BVs mostly Legs
: Cut. ulcers
• Livedo Reticularis.

Burst pattern of Livedo around leg ulcers ↓ CPAN

- HP
- LCV of (Small. Medium. sized BVs) ± Septal panniculitis.

* Treatment

- Etiolgy → Stop Drugs, Tt of HBV (IFNα + Vidaro-bin).
- Cut.: NSAIDs, Cs (Topical & Systemic), Colchicine
  Systemic: Systemic Cs & other Immunosuppressive (Dapsone).

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## Others

1. ~~Lymphomas~~ :
   - CTCL
   - CBCL

2 Types of TCL.

1. S.C. panniculitis like TCL (SPTL)
2. Nasal. Type NK/TCL (Nasal NKT)

↓

Both show S.C Nodules at leg & ± Trunk ± B Symptoms (Fever, Fatigue & W.t loss)

HP diff.

- SPLT: riming of fat cells by Mg Tcells.
- NK/TCL: Angiocentricity + agngio destruct + Necrosis.

Immunophenotyping

- SPLT: CD4+, EBV−
- NK/TCL: CD56, EBV+ve

Indolent Course ↑ SPLT

Aggressive ↑ NK/TCL

## ② EN-like lesions of Behcet-

to diff. from Classical lesions:

Ⓐ Clinically: at trunk, UL & buttocks.

Ⓑ HP: Lobular or Mixed Panniculitis
+
Vasculitis

---

## DD of Palmo-plantar Painful Nodules in Children (Painful-Plantar Erythema)

1. palmo-plantar EN
2. Acute traumatic urticaria (No s.c. affected) (AP)
3. Pseudomonas-Hot-feet Synd.
4. Recurrent PP Hidradenitis (Plantar Panniculitis)
   . HP: Neut. infilt. in Coil of Eccrine & dermis.
5. Cold panniculitis.

delayed-pressure ppt by physical Trauma

# • $\alpha_1$ - Antitrypsin deficiency panniculitis:

. Glycoprotein. produced by liver

. (F) [1] Tissue degradat$^{-}$
[2] Immuno Suppressive → ↓ inflammat$^{-}$.

. Cause of deficiency : Genetic.

Lower back buttocks Thighs

. C/P : large, Erythematous - Purpuric, Tender Nodules & plaques at lower Trunk & proximal extremities

→ Severe Necrosis & Ulcerat$^{-}$ ē oily discharge.

. others fever, Emphysema, Pulm. Embol., Angioedema

. Inv. (Lab) $\alpha_1$ Antitrypsin level. (< 5 mg/dl)

. (HP) Panniculitis ch BV (dermal & S.C.)

. Severe liquefactive Necrosis → Separat$^{-}$ of lobules from Septae.

. Hge, ± Vasculits.

. infil. early Neut. later Lymphocytes ē Histiocytes

. ~~H~~ → No effective H

(1) Tx → IV infusion of $\alpha_1$ antitrypsin.
6 mg/Kg/W → rapid Improvement

(2) Others: . Cs
. Dapsone
. Colchicine
. Doxy.

## • Cold Panniculitis

- d.t exposure to cold
- S.C Erythem. – Blush. Nodules
- Self limiting

## • Factitial P.

- Self inflicted by [Blunt Trauma / or inject= of drugs (Morphine, Pentazocin)]
- Chr., ulcerative, at thigh ass. ē woody indurat=.

Geometric ulcerat= عمل

## • Traumatic P.

4 Types of injury

- Cold Panniculitis
- Sclerosing – Lipogranuloma
- Injectable ##
- Blunt Trauma.
- Post irradiat= or radiat= recall dermatitis.

---

## • Infective Panniculitis:

- occurs in Immuno-Compromised
- Etiology
  1. Bact. ← G+ve / G-ve / Mycobact. (كل واحد)
  2. Viral: CMV
  3. Fungal: S.C & Systemic Types.
- HP: Neutrophilic lobular Panniculitis (± Septal)

## • Post-steroid

تعرض لأطفال
لو جرعة توقف
ضامن للكلى تزرق

## • lipoatrophic

- Autoimmune Type ass. ē Autoimmune dis (AICTD, R.A, DM) ⟶ Head ē Lipoatrophy.

---

## • Pancreatic P.: (Enzymatic)

- Pt. ē Pancreatic dis < Pancreatitis / Carcinoma
  - ⟶ Enzymes (Amylase, lipases, Trypsin)
  - ⟶ lobular Necrosis of S.C.T
- CIP(1). Systemic: fever, arthritis, abd. pain, Eosinophilia & pleural Effusion. (Visceral fat involvement)
  (2) Cut. S.C. Nodules (Tender or Asympt.) 1-3 ms Resolut= or ulcerat=: exude (Liquefactive Necrosis). ⟶ Thick brown oily Material

- Inv.: Serum
  - Lab: ↑ Amylase & lipases.
- HP: (1) Basophilic Necrosis (in Lupus P. ⟶ Eos. hyaline-Necrosis).
  (2) Ghost lipocytes: (lost-Nuclei + Shadowy Thick wall)
  (3) Saponificat=: Ca + fat (Basophilic material)
- ##: underlying Pancreatic problem (تهاب مزمن / حصوات / أورام Pancreatic)

## Panniculitides with needle-shaped clefts in the subcutis.

| Condition | Type of patient | C/P | Complications | Histopathology |
|---|---|---|---|---|
| **Sclerema neonatorum (SN)** | -Severely ill premature neonates<br>- 1st week<br>-Ppt by: hypothermia (also, asphyxia dehydration, defective complement) | - Cool, waxy, rigid and board-like skin<br>- Bad prognosis | - RD<br>- CHF<br>- Diarrhoea<br>- Death from septicemia, in three-fourths of cases | - Thickened fibrous septae<br>- Minimal inflammation and infilteration<br>- Needle-shaped clefts in lipocytes ONLY |
| **Subcutaneous fat necrosis of the newborn (SCFN) (Adiponecrosis subcutanea )** | -Full-term healthy<br>- 2-3 Ws<br>-Ppt by: Hypothermia (also,hypoglycemia due to gestational DM, meconium aspiration, preeclampsia) | - Discrete SC, firm movable nodules and plaques<br>- Excellent prognosis, self-limiting | -Hypercalcemia (onset may be delayed for several months, Causes seizures and nephrocalcinosis),<br>-Thrombocytopenia,<br>-Hypertriglyceridemia | -Lobular panniculitis<br>-Marked inflammation with granulomatous infilteration<br>- needle- shaped clefts (crystals) within lipocytes and giant cells;<br>-/+ calcification and Hge |
| **Poststeroid panniculitis** | -Children ( 1–14 ys)<br>- Ppt by: rapid withdrawal of corticosteroids (after 1-40ds). | As SCFN | Underlying conditions treated with systemic corticosteroids have included leukemia, cerebral edema, nephrotic syndrome, secretory diarrhea, acute rheumatic fever | As SCFN (but no calcification and Hge) |

**NB:** There are three entities–sclerema neonatorum, subcutaneous fat necrosis of the newborn, and poststeroid panniculitis–that are characterized histologically by formation of needle-shaped clefts within lipocytes. In contrast to adult fat, the subcutaneous fat of infants is thought to be prone to crystal formation because of a higher content of saturated fatty acids, including palmitic and stearic acids, and a relatively lower content of unsaturated fatty acids, such as oleic acid[68]. This increased saturated to unsaturated fatty acid ratio results in a higher melting point for stored fat and promotes crystallization under certain conditions. Microsized crystals (type A) apparently do not produce an inflammatory response; they are actually common (in a widely dispersed form) in healthy infants 6 months of age or less, but are more numerous in sclerema neonatorum. Larger, type B crystals that tend to be arranged in rosettes are capable of eliciting a granulomatous response; these crystal types are most often seen in subcutaneous fat necrosis of the newborn and poststeroid panniculitis[68,69]. Crystallization and defects in fat mobilization account for the clinical findings in these disorders.

Phagocytose other Cells ↓

# Cytophagic Histiocytic Panniculitis.

(. Donnez)
(. Emed.)

- Panniculitis ch BY infilt. by Histiocytes & other inflamm. cells → fat breakdown & Hge
  Engulfing of other cells (WBC (++), RBC) By Histiocytes.

- Cp ① Systemic
  - Fever
  - HSM — LCF / Jaundice
  - Pancytopenia (int. organ infilt by phagocytes).
  - Hge (GIT, Renal, RT)

  ② Cut. → Panniculitis.

- Etiology
  - Bg: Inf. (HSV), Immunosuppression, S.C TCL
  - Mg

- HP: . lobular (or Mixed) panniculitis
  . Infil.
  - Lymphocytes (+++)
  - Macrophages — Atypical, Enlarged, Engulf: RBC, WBCs, karyorrhectic debris [Bean-Bag Cells]
  - other cells

  Cytophagia

  . NB in cases of SC TCL → ē atypical cells do Immunophenotyping or TCR Gene analysis

- Tt
  - Cs
  - Ciclosporin
  - Dapsone
  - Chemotherapy. (CHOP)
  - IVIG.

# . Cold panniculitis

↓

. Type of Cold injury to S.C.T

**Etiopathogenesis** ( Types of patient ):

1. Newborn, Infants & children

d.t higher Saturated : Unsaturated Fatty acids

→ higher melting & solidifrate points

of Stored fat. → (4 Patterns)

(i). Ice therapy : 1st line tt of S.V. Tachycardia

(ii). SN

(iii). SCFN of Newborn (2wks)

(iv). children → Popsicle Panniculitis (< Cheeks, Chin)

2. Obese ♀ exposed to Cold → thighs, buttocks, & abdomen, arms, Chin.

3. Equestrian Panniculitis : exposure to Cold during Wearing tight-fitting Clothes. (فروسية)

4. Patients ē ← Perniosis & Paralyzed limbs

**CIP** : . Cold ex posure 2ds → < ± Systemic illness

Cut. lesions : firm. Hard, Erythem. Violaceous, illdefined, Cold, Painful. plaques & Nodules.

. Children : Popsicle Pannic at ..

. obese ♀ ??

. Paralyzed limb or limbs having Perniosis.

→ Site

See below → . SN & SCFN

**HP**

Lobular (± Septal) Panniculitis.

Mucin deposits (Alcian blue) [No Needle Clefts except in <]

Patchy lymphohistiocytic infilt. ē Eos.

**TT**

. most Self limiting

. rewarming

. Systemic tt

. Topical tt.